**Assessment of steroid use as a key performance indicator in inflammatory bowel disease - analysis of data from 3561 UK patients**

*Steroid excess in IBD*

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CPS, GCP and TR designed the study. All authors contributed equally to data collection and interpretation of results. CPS, GCP and TR analysed the data and wrote the draft manuscript. All other authors critically reviewed the manuscript.

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**Abstract**

**Background:**

Patients with IBD are at risk of excess corticosteroids.

**Aims**

To assess steroid excess in a large IBD cohort and test associations with quality improvement and prescribing.

**Methods**

Steroid exposure was recorded for outpatients attending 19 centres and associated factors analysed. Measures taken to avoid excess were assessed.

**Results**

Of 2385 patients, 28% received steroids in the preceding 12 months. 14.8% had steroid excess or dependency. Steroid use was significantly lower at ‘intervention centres’ which participated in a quality improvement programme (exposure: 23.8% vs 31.0%, p<0.001; excess 11.5% vs 17.1%, p<0.001). At intervention centres, steroid use fell from 2015 to 2017 (steroid exposure 30.0% to 23.8%, p=0.003; steroid excess 13.8% to 11.5%, p=0.17). Steroid excess was judged avoidable in 50.7%. Factors independently associated with reduced steroid excess in Crohn’s disease (CD) included maintenance with anti-TNF agents (OR 0.61 (0.24 – 0.95)), treatment in a centre with a multi-disciplinary team (OR 0.54 (0.20 – 0.86)) and treatment at an intervention centre (OR 0.72 (0.46 – 0.97)). Treatment with 5-ASA in CD was associated with higher rates of steroid excess (OR 1.72 (1.24 – 2.09)). In ulcerative colitis (UC), thiopurine monotherapy was associated with steroid excess (OR 1.97 (1.19 – 3.01)) and treatment at an intervention centre with less steroid excess (OR 0.72 (0.45 – 0.95)).

**Discussion**

This study validates steroid assessment as a meaningful quality measure and provides a benchmark for this performance indicator in a large cohort. A programme of quality improvement was associated with lower steroid use.

**Key words:**

Inflammatory bowel disease, Crohn’s disease, ulcerative colitis, corticosteroids,

quality indicator, key performance indicator

**Background:**

Despite significant advances in both our understanding and treatment of inflammatory bowel disease (IBD) corticosteroids remain a mainstay of treatment. Although an effective induction agent, steroids have no role as a maintenance agent and prolonged exposure can lead to a range of significant morbidities.1-3 In both Europe and the USA patient organisations have suggested that steroid free remission should be a key therapeutic target.4-6 Several international studies have shown that around 30-50% of patients continue to be exposed to corticosteroids each year, with around 10-20% exposed to significant excess corticosteroids, which was potentially avoidable in around half of these cases of excess. 4,7-9 Despite significant advances in therapeutics steroid prescription rates have remained static over the last two decades. 10,11

In 2015, as part of a national quality improvement project evaluating excess steroid exposure in UK IBD patients, we demonstrated that a number of service and patient level factors independently correlated with risks of excess steroid exposure.4 Subsequently, centres participating in the quality improvement project undertook a series of measures including patient and physician education, reopening of telephone helplines and rapid access clinics with a goal of removing barriers to specialist advice for patients and reducing inappropriate steroid excess. Around the same time, significant changes to the prescribing landscape in IBD occurred. In particular, in the UK, the National Institute for Health and Care Excellence (NICE) for the first time gave approval for the use of biologic therapies in ulcerative colitis (UC) (including both anti-tumour necrosis factor (anti-TNF) therapy12 and the anti-integrin agent Vedolizumab13) whilst vedolizumab was approved for use in patients with Crohn’s disease (CD) refractory to anti-TNF therapy.14

The goals of the present study were therefore to validate our previous observations regarding the incidence and correlates of excess steroid exposure in a new cohort of UK patients, including 11 centres who had not been involved in the previous quality improvement project with the aim of providing further data to help establish a benchmark for steroid excess as a Key Performance Indicator. In particular, we wanted to capture any impact of participation in the quality improvement project as well as of changes in NICE guidance relating to biologics in IBD on rates of steroid excess.

**Methods:**

*Study centres and patient recruitment*

Using a previously developed online assessment tool for steroid exposure in patients with IBD4 we prospectively collected data from IBD patients attending outpatient clinics over 3 months between April-July 2017. The participating sites worked with a standard operating procedure which required them to enrol all consecutive patients with IBD attending face to face clinics without patient selection beyond basic inclusion criteria (box 1). These criteria were: adult patients with a confirmed diagnosis of IBD based on internationally accepted clinical, endoscopic, histological and or radiological criteria.2,15 Only patients with an established diagnosis and a minimum of 3 months disease duration were included; there were no other exclusion criteria. Treating clinicians were asked to categorise disease severity at the time of the clinic visit based upon a physician global assessment (PGA) using a score of 0-3. Participants were asked a standard set of questions about their IBD, further data were gathered from hospital and where accessible general practitioner’s records. The steroid assessment was brief to allow ‘live’ use in busy clinical environments and hence we did not routinely collect data on age, sex, disease duration or IBD phenotype.

Recruitment occurred at 19 geographically and clinically diverse centres in England, Wales and Scotland. We divided the centres into those (intervention group) who took part in the 2015 audit and subsequently conducted local quality improvement programmes aiming at reducing steroids excess (7 centres) and those who were either new to the steroid assessment process (11 centres out of 20 approached agreed participation) or where no quality improvement programme occurred (1 centre). The latter formed the non-intervention group of 12 centres. Centre characteristics are displayed in table 1. Data were stored and transmitted securely within National Health Service operated IT infrastructure.

*Study procedures*

The review of steroid use was standardized in the study. Inclusion criteria were consecutive adult out-patients with a confirmed diagnosis of IBD based on internationally accepted clinical, endoscopic, histological and or radiological criteria. The only exclusion criteria were patients with a diagnosis of less than 3 months disease duration. All patients were asked “Have you used/been prescribed steroids in the 12 months (from the date of the clinic visit), either from clinic, the emergency department, your GP or from home supplies?” If the answer was yes, then the following supplementary questions were asked:

1. Were the steroids prescribed for your IBD? If not, why were they prescribed?

2. How long was the course of steroids?

3. How many courses of steroids did you take?

4. Where you able to stop the steroids without a return of your symptoms?

In addition, hospital records were examined to see whether there was any documentation of steroid prescription in the last year.

*Steroid use and definitions*

To allow for comparison with the 2015 study we used the same definitions as detailed previously.4 In short we recorded steroid exposure (number of courses, length of the longest course, ability to taper, flares on or within 3 months of withdrawal) for the 12 month period preceding the clinic visit. As in 2015 we defined steroid dependency or excess in accordance with ECCO and UK guidelines as the presence during the 12 month period preceding the clinic visit of 1 or more of: (i) the prescription of >1 steroid course or (ii) inability to wean steroids below 10mg/day prednisolone or 3mg/day budesonide within 3 months of starting steroids or (iii) disease flare within 3 months of stopping steroids.15-17

To judge the avoidability of steroid excess we peer reviewed all cases meeting the criteria for steroid dependency or excess in a selection of centres, comprising all centres in the intervention group as well as 1 centre in the non-intervention group. For these cases relevant clinic letters, biochemical parameters and endoscopy reports were collated and anonymised, before being centrally allocated for fully blinded peer review by an investigator from a different centre. Each case was assigned to the same pre-defined 4 categories as in 2015: (i) non-IBD prescribing; (ii) prescribing where no alternative existed or where appropriate measures to avoid steroid dependency or excess were put in place; (iii) prescribing where relevant alternatives were sub-optimally explored; (iv) prescribing where relevant alternatives were not explored. Where the peer reviewer felt unable to categorise, further adjudication was performed independently by 2 blinded central reviewers and results reconciled where necessary.

*Analysis plan*

Data on steroid use and avoidability were combined with other patient data for descriptive analysis. All statistical tests were performed using R (version 3.5.1).18 Between-group comparisons of outcomes were performed using Fisher’s exact test. Associations between steroid dependency or excess, avoidability and patient as well centre based organisational factors were combined and analysed using mixed effects logistic regression analysis with (i) steroid dependency or excess, or (ii) inappropriate steroid excess as a binary outcome variable and treatment centre modelled as a random effect. We reviewed several potential explanatory variables including data on disease severity, drug prescriptions, hospital type, physician and IBD nurse staffing levels (corrected per capita), service models including joint medical/surgical and dedicated IBD clinics as well as IBD MDT meetings, and availability of IBD clinic ‘flare’ (short notice) slots. Model selection was performed by sequential testing with optimisation of the Akaike information criterion with preference given for more parsimonious models. Confidence intervals were determined using a multilevel bootstrap approach.

*Ethics approval and consent exemption*

The study was conducted as a prospective multi-centre clinical audit and no identifiable data were collected outside the individual study centres. Relevant clinical audit authorisation was obtained in participating centres. Due to the nature of audit, research ethics committee approval and informed consent were not required.

**Results:**

*Patient cohort*

The total cohort consisted of 2385 patients of which 1006 were recruited from the intervention group sites and 1379 from the non-intervention group sites. There were no incomplete data and all cases were used for analysis. The recorded diagnoses were 45.8% CD, 51.3% UC, 2.9% IBD-unspecified (IBD-U) for the intervention and 47.1% CD, 48.9% UC and 4.0% IBD-U for the non-intervention group.

Details for the patient cohorts including drug exposure can be found in table 2. According to Physician Global Assessment 76.8% of the overall cohort were in remission/mild disease, 20.1% had moderate and 3.1% had severe disease. The cohort of patients with moderate severe disease therefore consisted of 553 patients: CD 281 (25.3% of CD cohort), UC 249 (20.9% of UC cohort) and IBD-U 23 (27.4% of IBD-U cohort). Patients with CD or UC from non-intervention group sites were more likely to be judged as having moderate disease severity than patients from intervention group sites (26.0% and 24.0% of CD and UC cohort at non-intervention group sites, compared to 15.6% and 10.7% of CD and UC cohort at intervention group sites; p<0.01 for both comparisons, see table 2).

639 (26.8%) patients were on current biologic therapy, of which 570 (23.9%) were on anti-TNF and 69 (2.9%) were on anti-integrin. Monotherapy with a biologic but no immunomodulator was recorded in 296 patients (46.3% of patients on a biologic). Prior but not current anti-TNF exposure was recorded in a further 215 (9.0%). Current anti-TNF therapy was more common in patients with CD than UC (36.8% vs 12.0%, p<0.01). 896 (37.6%) of patients were currently on immunomodulator therapy, including 343 (14.4%) of patients using an immunomodulator in combination with a biologic.

*Steroid use*

In the overall cohort 667 patients (28.0%) were exposed to steroids in the preceding 12 months. Steroid exposure for CD and UC was similar (26.7% vs 28.2%) but was significantly higher for IBD-U (41.7%, p=0.006 vs CD/UC.) Steroid excess occurred in 352 patients in total (14.8% of total cohort; CD 15.0%, UC 13.8%, IBD-U 25%; p=0.02).

Patients met the criteria for steroid excess due to >1 course of steroids in 12 months (227 patients; 64.5% of all patients receiving steroid excess), a course of steroids exceeding 3 months (180 patients; 51.1%) and disease flare on tapering steroid doses or shortly after cessation (244 patients; 69.3%). 63.9% of patients receiving excess steroids met >1 criterion with 21.0% of patients meeting all 3 criteria (Figure 1).

Within the cohort of moderate/severe disease, 352 patients (63.6%) were exposed to steroids (CD 59.1%, UC 66.7%, IBD-U 87.0%). In the same cohort, steroid excess was recorded in 230 patients (41.6%) representing 39.5%, 42.1%, 60.9% of the moderate/severe CD, UC and IBD-U cohorts respectively.

*Avoidability of steroid excess*

We previously demonstrated that approximately 50% of patients with steroid excess received appropriate clinical care, while the other 50% had avoidable or potentially avoidable steroid excess.4 Therefore, we used the same tests of avoidability as part of a detailed, blind peer review of case records to evaluate efforts to avoid steroid excess.

We identified 156 cases of steroid excess amongst records for 1131 patients from those centres participating in the in-depth review process. In 16 cases relevant notes were not recovered, whilst in a further 2 cases recovered notes were incomplete, leaving full data available for 138 cases (71 CD, 61 UC, 6 IBD-U). In 18 of these cases, initial peer review did not reach a clear decision regarding avoidability, leading to a process of independent adjudication and reconciliation by 2 further peer reviewers.

Steroid prescriptions for non-IBD indications were found in 4 patients (2.9%), whilst appropriate treatment attempting to avoid excess or the absence of valid alternatives to steroids was noted in 64 (46.4%) (Figure 2). This gave a combined figure for appropriate steroid excess within the group receiving excess steroids of 49.3%. Conversely, 50.7% of patients were deemed to have received inappropriate excess steroids (either definitely avoidable (56 patients, 40.6%) or probably avoidable (14 patients, 10.1%)). This resulted in an annual incidence within the cohort of 6.2% of inappropriate steroid excess.

For patients with steroid excess, the rate of inappropriate excess was similar between CD and UC subgroups (53.5% vs 49.2%, p=0.73). This was also true when considering just the cohort of patients with moderate/severe disease. Likewise, for patients receiving steroid excess, age did not appear to affect the appropriateness of the prescription (data not shown).

We were able to identify fully the type of steroid prescribed in 116 cases (84.0%). In 88 (75.9%) cases prednisolone was the sole oral steroid prescribed whilst in 16 (13.8%), budesonide was the sole oral steroid prescribed. In 12 (10.3%) cases both prednisolone and budesonide were prescribed. In 126 cases (91.3%) we were able to accurately identify the source of all steroids taken. Of these, 19.8% of cases involved at least one steroid prescription originating from primary care, whilst 73.9% of cases involved steroid prescriptions generated solely from the responsible secondary care centre (the remaining 6.4% of cases involved alternative additional sources, such as private practice or from referring hospitals no longer involved in the patient’s care). Cases where steroid prescriptions were all generated from secondary care were less likely to be classed as inappropriate excess than those cases where at least one prescription originated in general practice (43.0% vs 68.0%, p=0.04).

*Differences between sites and over time*

Rates of steroid exposure and excess were significantly lower in intervention sites than in non-intervention sites (exposure: 23.8% vs 31.0%, p<0.001; excess 11.5% vs 17.1%, p<0.001). These differences were significant for comparisons within both UC and CD populations. Since patients from non-intervention sites were more likely to be judged as having moderate/severe disease, we tested the correlation between rates of steroid excess and the percentage of patients judged to have moderate or severe disease at each centre (supplementary figure 1A-C). We found modest but significant correlation. When we restricted analysis to those subgroups of patients having moderate/severe disease only, we saw more consistent rates of steroid excess between centres but still some variation (supplementary figure 1D-I). This suggested that although disease severity was an important determinant of outcome, other factors might be affecting rates steroid excess.

Likewise, we noted differences in rates of steroid exposure and excess between 2015 and 2017 at sites within the intervention group. Total steroid exposure fell from 30.0% to 23.8% (p=0.003) and steroid excess from and 13.8% to 11.5% (p=0.17). However, there was an accompanying trend towards a lower disease activity for the patients seen at these centres, with an overall decrease in the proportion of patients recorded as having moderate/severe disease from 21.2% in 2015 to 15.2% in 2017 (p=0.001, Supplementary table 1). Analysis of steroid exposure rates in moderate/severe patients only showed a trend towards lower rates from 2015 to 2017 that did not reach statistical significance (66.1% vs 60.1%).

*Changes in drug use*

Since reimbursement rules set by NICE were changed substantially between the time of the 2015 and 2017 audit cycles, we were interested in examining the impact of these changes on medications that outpatients were exposed to. Use of anti-integrin therapy for both CD and UC remained low within the cohort (table 2), as did use of anti-TNF agents for UC. For those centres contributing data to both 2015 and 2017 audits, current use of anti-TNF therapy in the total population increased numerically but not significantly (19.4% increasing to 22.9%, p=0.08). Within the UC cohort, the increase from 2015 to 2017 was also not significant (from 9.6% to 11.6%,p=0.33). Within the moderate/severe population, there was a numerical increase in anti-TNF usage for both CD and UC cohorts that did not reach significance (CD 37.1% 2015, 41.7% 2017; UC 20.6% 2015, 25.8% 2017). Use of anti-integrin therapy within these centres remained low across all populations.

*Associations with clinical and organisational factors*

Although there were differences in terms of steroid exposure and excess for patients treated at intervention and non-intervention sites, there were also important baseline differences between the patient groups including disease severity and drug exposure. We therefore used a mixed effects logistic regression analysis to test association with steroid outcomes for a number of patient-level (e.g. disease severity, medication history) and service-level factors (e.g. hospital type, staffing levels, IBD service configuration, quality improvement participation) (table 3).

Disease activity was a strong independent correlate of steroid excess for both UC and CD. Other factors showing independent correlation with risk of steroid excess in CD included receipt of maintenance therapy with anti-TNF agents (>3 months, OR 0.61 (0.24 – 0.95)). Conversely treatment with 5-ASA in CD was associated with a higher rate of steroid dependency or excess (OR 1.72 (1.24 – 2.09)). For CD patients treatment in an IBD centre with an MDT (OR 0.54 (0.20 – 0.86)) and treatment in a centre that took part in the quality intervention (OR 0.72 (0.46 – 0.97)) were both associated with a reduced risk of steroid dependency / excess.

For patients with UC, in addition to disease activity, we identified that maintenance therapy with thiopurine without receipt of a biologic (>3 months) was independently associated with risk of steroid excess (OR 1.97 (1.19 – 3.01)). In UC patients, treatment in a centre that took part in the quality intervention was associated with a reduced risk of steroid dependency / excess (OR 0.72 (0.45 – 0.95)).

We used the outcomes of in depth case review to test of correlates of inappropriate steroid excess. Since these cases were drawn predominantly from centres in the intervention group, we did not test the effects of participation in the quality improvement process. For both UC and CD, disease activity was again correlated with increased risk of inappropriate excess, and treatment in a centre that had an active IBD MDT was associated with decreased risk of inappropriate excess (CD: OR 0.37 (0.15-0.83); UC: OR 0.24 (0.07-0.73)).

As a sensitivity analysis for the effects of difference case mix between centres, we repeated the regression analysis using only patients classified as having moderate/severe disease. For the CD model, all fitted variables including treatment at a centre in the intervention group, remained significant predictors of steroid excess. For the UC model, treatment at a centre in the intervention group was no longer a significant predictor of steroid excess when considering this moderate/severe subgroup alone.

**Discussion:**

In our study of 2385 outpatients with IBD, 14.8% had received exposure to steroids in excess of international guidelines in the previous 12 months, and in half of these cases this excess was potentially avoidable. These findings are strikingly similar to data from our previous UK study, and through the addition of multiple participating centres, suggests that our previous findings may be applicable to wider IBD cohorts.4 Indeed, similar rates of corticosteroid exposure and excess have been reported in other international cohorts from the USA,8 the Netherlands,19 the UK,10 Canada and Germany.20

We demonstrated that steroid excess could be easily and robustly measured in routine clinical practice (e.g. using an online assessment tool4). In addition, steroid use is known to be positively correlated with adverse outcomes. 21,22 Taken together, this supports the idea that excess steroid use may be a useful key performance indicator for IBD with which to evaluate a service and drive standards for patients. Such key performance indicators have previously been lacking in IBD, unlike other disease areas such as diabetes23,24 and cardiovascular disease25. Indeed, the 2019 UK IBD standards have included steroid exposure as a quality marker.26

Importantly, despite the static headline rates of steroid exposure between 2015 and 2017 in our work, our current study suggested that steroid exposure might be reduced. This would be another critical feature for a key performance indicator.27 In the intervention sites a number of changes were introduced, which were tailored to the local needs of the service. These included feedback of the audit findings to departmental meetings, along with direct referral pathways from primary care, ring-fenced outpatient clinic slots for flares and urgent reviews, re-opening of a patient telephone helpline, education for primary and secondary care clinicians and written patient information on steroids. These measures were associated with a reduction in total steroid exposure from 30.0% to 23.8% (p=0.003) and a numerical reduction in steroid excess from and 13.8% to 11.5% (p=0.17). However, there were significant changes in case mix at these centres over time which limit interpretation of these findings. In particular, the proportion of patients with moderate/severe disease reduced, whilst usage of anti-TNF therapy increased within the moderate/severe cohort. Nonetheless, when restricting analysis of steroid exposure to within the moderate/severe cohort, the observed trend towards lower exposure rates persisted.

Likewise, our observation of lower rates of steroid exposure and excess for patients treated at intervention sites was potentially confounded by differences in baseline disease severity and drug exposure between the cohorts. Therefore, through logistic regression analysis, we were able to look for variables independently associated with risk of steroid excess.

Logistic regression allows us to test the effects of multiple potentially contributory variables simultaneously, and can, to some extent, correct for differences in baseline characteristics between patients and centres. A major limitation was that the biggest effect size came from a variable that was captured in a well-recognised but crude manner at a single timepoint – namely disease severity recorded using a PGA score. Given that defining disease severity in IBD is fraught with difficulty, this was a necessary compromise for this study, but raises the possibility of unmeasured effects of further differences in patient profiles.

Perhaps unsurprisingly, in addition to differences associated with disease severity, the use of medical strategies of proven efficacy did independently correlate with steroid outcomes, with, for example, reduced rates of steroid excess seen with use of anti-TNF for CD, compared to increased rates seen with use of 5-ASA for CD, a maintenance strategy backed neither by evidence or guidelines.15,28 In addition, both for patients with CD and UC, treatment at an intervention site was independently associated with reduced risk of excess steroid exposure. We also demonstrated that for CD patients treatment in a centre with an IBD MDT there was an independent association with reduced risk of steroid excess, in keeping with our previous observations in this regard. In a sensitivity analysis to see if the observed effects persisted when analysing patients with moderate/severe disease only, we were able to replicate all our observed correlations for patients with CD but not UC. Since this study was not designed to look at just the subgroup alone, this might reflect an underpowered analysis.

Since the time of our 2015 audit, the therapeutic options for IBD patients in the UK increased as NICE approved biologic therapies (anti-TNF12 and vedolizumab)13 for UC and vedolizumab for CD refractory to anti-TNF therapy.14 Exposure to vedolizumab in the current study remained low and we were therefore unable to examine whether vedolizumab treatment was associated with a reduction in the risk of steroid excess. Increases in anti-TNF usage were also perhaps surprisingly modest, given the major shifts in reimbursement. For those sites providing data in both 2015 and 2017, current usage of anti-TNF for CD rose from 30.0% to 34.1% (p=0.2), while the use in UC increased from 9.6% to 11.6% **(**p=0.33).

The major strength in the current study is the cohort size and the data from 1379 new patients from sites not involved in the previous study, validating our initial findings from 2015. Utilisation of the steroid assessment tool has been shown to be a rapid, straight forward and pragmatic measure of quality in IBD and applicable to the wider IBD community. This is further supported by recent publications from other centres.1,7,8 Furthermore our current study has confirmed the most important factors associated with steroid excess identified in our earlier cohort.4

There are a number of limitations to our study. We used an online tool to capture steroid exposure data in real time in a clinical setting. As a consequence, our data do not provide enough granularity to determine the exact cause of steroid excess in every case, nor to determine the effects of other patient variables such as sex, age, disease duration and IBD phenotype. It is also possible that we under-estimated steroid exposure in our cohort since we did not have full access to primary care prescribing records. Additionally, patients with a disease duration of less than one year were not excluded and hence may have led to a further underestimation of steroid burden across a 12 month period. Interestingly, there were no cases with a disease duration shorter than one year included in the in depth review cohort. Despite the limitations the SAT is a simple, pragmatic tool which allows direct comparisons between centres.

Since the data capture tool was used in a clinical setting, it is important to be confident in the accuracy of data obtained. In this regard, during the in depth review we did not note any cases where patients had been incorrectly coded as experiencing steroid excess. We do, however, lack data on interobserver variation and it remains possible that there were cases of steroid excess that were not captured for in-depth review.

We have demonstrated that participation in a quality improvement program was associated with a reduction in steroid excess. Centres were not randomised to intervention vs. non-intervention group participation and there may have been other characteristics of the centres that underlined the differences we observed. Nevertheless, we were not able to detect association with a number of other variables we tested, including hospital type (e.g. teaching hospital vs general; number of gastroenterologists, gastroenterology trainees or IBD nurses (either absolute or corrected per capita)).

Owing to the nature of different local service set-ups the quality improvement intervention was not a uniform approach but was designed locally to the needs of each individual centre, with regular meetings of investigators from involved centres to share experience and strategies. None of this demonstrates causality, indeed it would be wrong to claim that any single intervention caused a reduction in steroid excess, but it is interesting to note that in our cohort it was shifts in physician participation in steroid audit and service configurations, rather than major shifts in prescribing behaviour that appeared to correlate with the modest changes in steroid exposure and excess seen.

The proposed use of steroid excess assessment as marker of quality relies on using the simple definition of steroid dependency/excess as by ECCO thereby both capturing cases where difficult to treat disease led to steroid excess as well as cases where poor IBD management led to the excess use of steroids with a consistent rate of around 50% for each category in both audit periods. In our opinion the use of the ECCO definition allows for simple and easy audits of practice in a similar fashion to the use of caecal intubation rates as a measure of colonoscopy quality.

In conclusion, we have demonstrated that steroid excess can be captured in a robust, reliable and practical manner and that quality improvement programmes appear to be associated with a reduction in steroid excess. This advances the case for steroid excess as a potential key performance indicator of quality in an IBD service, although in order for clinicians to benchmark their service and provide targets for improvements, any numerical goal attached to this key performance indicator would require consideration of case mix. Further data, including from national and international contexts is needed.

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**Table 1: Organisational characteristics of participating centres**

IBD MDT: IBD multi-disciplinary team

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | | |  | |  | | |  | | |  |  |  |  |  |  |
| Group | **Status** | **Population** | **Gastroent-erologists** | **IBD nurses** | | **Gastroent-erology trainees** | | **IBD MDT** | **dedicated IBD clinics** | | **combined surgical clinics** |
| Intervention | District General Hospital | 350,000 | 8 | 2 | | 1 | | yes | yes | | yes |
| Intervention | Teaching Hospital | 800,000 | 10.5 | 4.5 | | 10 | | yes | yes | | yes |
| Intervention | Teaching Hospital | 1,000,000 | 6.8 | 2.5 | | 5 | | yes | yes | | no |
| Intervention | Teaching Hospital | 484,000 | 9 | 2 | | 4 | | yes | yes | | yes |
| Intervention | Teaching Hospital | 445,000 | 3.5 | 0.9 | | 2 | | yes | yes | | no |
| Intervention | Teaching Hospital | 420,000 | 7 | 2 | | 4 | | yes | no | | no |
| Intervention | Teaching Hospital | 450,000 | 7 | 2 | | 5 | | yes | yes | | yes |
| Non-intervention | District General Hospital | 820,000 | 11 | 2 | | 5 | | no | yes | | no |
| Non-intervention | District General Hospital | 350,000 | 8 | 2 | | 2 | | yes | yes | | no |
| Non-intervention | District General Hospital | 165,000 | 5 | 3 | | 2 | | yes | yes | | yes |
| Non-intervention | District General Hospital | 300,000 | 6.5 | 1.8 | | 2 | | yes | yes | | yes |
| Non-intervention | District General Hospital | 500,000 | 11 | 2 | | 2 | | yes | no | | no |
| Non-intervention | District General Hospital | 250,000 | 4 | 1 | | 1 | | yes | yes | | no |
| Non-intervention | District General Hospital | 430,000 | 7 | 1 | | 2 | | no | no | | no |
| Non-intervention | Teaching Hospital | 1,500,000 | 12 | 4 | | 3 | | yes | yes | | yes |
| Non-intervention | Teaching Hospital | 350,000 | 11 | 2.6 | | 3.6 | | yes | yes | | yes |
| Non-intervention | Teaching Hospital | 500,000 | 4 | 2.2 | | 2 | | yes | yes | | yes |
| Non-intervention | Teaching Hospital | 1,000,000 | 12 | 2 | | 4 | | yes | yes | | yes |
| Non-intervention | District General Hospital | 700,000 | 14 | 2 | | 5 | | yes | yes | | no |

**Table 2: Study cohort composition regarding IBD diagnosis, severity , previous and current IBD treatments**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Intervention group n(%)** | | | | **Non-intervention group n(%)** | | | | **Statistical tests** | | | |
|  | CD | UC | IBD-U | Total | CD | UC | IBD-U | Total | CD | UC | IBD-U | Total |
| **Total patients** | 461 (45.8) | 516 (51.3) | 29 (2.8) | 1006 (100) | 650 (47.1) | 674 (48.9) | 55 (4.0) | 1379 (100) | 0.53 | 0.25 | 0.18 | NA |
| **Disease severity** |  |  |  |  |  |  |  |  |  |  |  |  |
| -Remission | 216 (46.9) | 299 (57.9) | 14 (48.3) | 529 (52.6) | 267 (41.1) | 278 (41.2) | 25 (45.5) | 570 (41.3) | 0.06 | **<0.01** | 0.82 | **<0.01** |
| -Mild | 161 (34.9) | 155 (30.0) | 8 (27.6) | 324 (32.2) | 186 (28.6) | 209 (31.0) | 14 (25.5) | 409 (29.7) | **0.03** | 0.75 | 1.00 | 0.19 |
| -Moderate | 72 (15.6) | 55 (10.7) | 7 (24.1) | 134 (13.3) | 169 (26.0) | 162 (24.0) | 15 (27.3) | 346 (25.1) | **<0.01** | **<0.01** | 0.80 | **<0.01** |
| -Severe | 12 (2.6) | 7 (1.4) | 0 (0) | 19 (1.9) | 28 (4.3) | 25 (3.7) | 1 (1.8) | 54 (3.9) | 0.14 | 0.02 | **<0.01** | **<0.01** |
| **Drug exposure (current or prior)** |  |  |  |  |  |  |  |  |  |  |  |  |
| -5ASA | 269 (58.4) | 511 (99.0) | 26 (89.7) | 806 (80.1) | 436 (67.1) | 646 (95.8) | 46 (83.6) | 1128 (81.8) | **<0.01** | **<0.01** | 0.53 | 0.31 |
| -Thiopurine | 345 (74.8) | 218 (42.2) | 13 (44.8) | 576 (57.3) | 475 (73.1) | 324 (48.1) | 26 (47.3) | 825 (59.8) | 0.53 | **0.05** | 1.00 | 0.22 |
| -Other IM | 56 (12.1) | 21 (4.1) | 2 (6.9) | 79 (7.9) | 116 (17.8) | 43 (6.4) | 8 (14.5) | 167 (12.1) | **0.01** | 0.09 | 0.48 | **<0.01** |
| -Anti-TNF | 215 (46.6) | 75 (14.5) | 9 (31.0) | 299 (29.7) | 344 (52.9) | 132 (19.6) | 15 (27.3) | 491 (35.6) | **0.04** | 0.07 | 0.80 | **<0.01** |
| -Anti-integrin | 11 (2.4) | 6 (1.2) | 0 (0.0) | 17 (1.7) | 23 (3.4) | 26 (3.9) | 3 (5.5) | 55 (4.0) | 0.30 | **<0.01** | 0.54 | **<0.01** |
| **Drug exposure (current only)** |  |  |  |  |  |  |  |  |  |  |  |  |
| -5ASA | 116 (25.2) | 449 (87) | 19 (65.5) | 584 (58.1) | 182 (28) | 512 (76) | 19 (34.5) | 713 (51.7) | 0.30 | **<0.01** | **0.01** | **<0.01** |
| -Thiopurine mono | 102 (22.1) | 106 (20.5) | 3 (10.3) | 211 (21) | 122 (18.8) | 162 (24) | 10 (18.2) | 294 (21.3) | 0.17 | 0.16 | 0.53 | 0.88 |
| -Other IM mono | 9 (2) | 4 (0.8) | 0 (0) | 13 (1.3) | 16 (2.5) | 11 (1.6) | 3 (5.5) | 30 (2.2) | 0.68 | 0.29 | 0.55 | 0.12 |
| -Anti-TNF mono | 68 (14.8) | 15 (2.9) | 5 (17.2) | 88 (8.7) | 127 (19.5) | 41 (6.1) | 6 (10.9) | 174 (12.6) | **0.04** | **0.01** | 0.50 | **<0.01** |
| -Anti-integrin mono | 6 (1.3) | 4 (0.8) | 0 (0) | 10 (1) | 13 (2) | 9 (1.3) | 2 (3.6) | 24 (1.7) | 0.48 | 0.41 | 0.54 | 0.16 |
| -Anti-TNF combo | 89 (19.3) | 45 (8.7) | 3 (10.3) | 137 (13.6) | 125 (19.2) | 42 (6.2) | 4 (7.3) | 171 (12.4) | 1.00 | 0.12 | 0.69 | 0.39 |
| -Anti-integrin combo | 5 (1.1) | 2 (0.4) | 0 (0) | 7 (0.7) | 13 (2) | 14 (2.1) | 1 (1.8) | 28 (2) | 0.34 | **0.01** | 1.00 | **0.01** |
|  |  |  |  |  |  |  |  |  |  |  |  |  |

**Table 3: Independent predictors significantly associated with steroid dependency or excess and inappropriate steroid excess using mixed effects logistic regression analysis for UC and CD**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Ulcerative colitis** | | | | |
|  | **all excess exposure** | | **inappropriate excess** | | |
| Factor | OR (95% CI) | p value | OR (95% CI) | | p value |
| Moderate/severe disease activity | 14.28 (7.26-34.04) | <2x10-16 | 10.29 (3.67-35.92) | | 1.2x10-7 |
| Thiopurine (maintenance monotherapy) | 1.97 (1.19-3.01) | 0.04 |  | |  |
| Intervention centre | 0.72 (0.45-0.95) | 0.03 | *Not tested* | | |
| Anti-TNF (maintenance) |  |  |  | |  |
| 5-ASA |  |  |  | |  |
| Multi-disciplinary team |  |  | 0.24 (0.07-0.73) | | 0.006 |
|  | **Crohn’s Disease** | | | | |
|  | **all excess exposure** | | | **inappropriate excess** | |
|  | OR (95% CI) | p value | OR (95% CI) | | p value |
| Moderate/severe disease activity | 6.79 (3.80-13.05) | <2x10-16 | 14.25 (5.97-44.45) | | 5.03x10-9 |
| Thiopurine (maintenance monotherapy) |  |  |  | |  |
| Intervention centre | 0.72 (0.46-0.97) | 0.03 | *Not tested* | | |
| Anti-TNF (maintenance) | 0.61 (0.24-0.95) | 0.03 |  | |  |
| 5-ASA | 1.72 (1.24-2.09) | 0.01 |  | |  |
| Multi-disciplinary team | 0.54 (0.20-0.86) | 0.02 | 0.37 (0.15-0.83) | | 0.02 |

***Figure and table legends:***

*Figure 1: Venn diagram of clinical reasons for triggering steroid dependency / excess criteria highlighting that many patients met more than one criterion*

*Figure 2: Overview of steroid dependency / excess and breakdown by avoidability in patients with IBD*

*Table 1: Organisational characteristics of participating centres*

*Table 2: Study cohort composition regarding IBD diagnosis, severity , previous and current IBD treatments*

*Table 3: Independent predictors significantly associated with steroid dependency or excess and inappropriate steroid excess using mixed effects logistic regression analysis for UC and CD*

**Box 1**