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Real-life anti-Tumour necrosis factor experience in > 500 paediatric United Kingdom Inflammatory Bowel Disease patients

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ABSTRACT

Objectives: To measure the effectiveness, safety and use of anti-Tumour necrosis Factor (TNF) therapy in paediatric inflammatory bowel disease (PIBD) in the United Kingdom (UK).

Methods: Prospective UK audit of patients newly starting anti-TNF therapy. Disease severity was assessed using Physician Global Assessment (PGA) +/or the Paediatric Crohn's Disease Activity Index (PCDAI).

Results: 37 centres participated (23 of 25 specialist PIBD sites). 524 patients were included; 429 Crohn's disease (CD), 76 ulcerative colitis (UC), 19 IBD unclassified (IBDU). 87% (488/562) anti-TNF was infliximab; commonest indication was active luminal CD 77% (330/429) or chronic refractory UC/IBDU 56% (53/95); 79% (445/562) had concomitant co-immunosuppression. In CD (267/429 male), median time from diagnosis to treatment was 1.42 years (IQR 0.63-2.97). Disease (at initiation) was moderate or severe in 91% (156/171) by PGA compared to 41% (88/217) by PCDAI; Kappa (K) 0.28 = only 'fair agreement' ($p<0.001$).

Where documented, 77% (53/69) of CD patients responded to induction; and 65% (46/71) entered remission. 2287 infusions and 301.96 years of patient follow-up (n=385) are represented; adverse events affected 3% (49/1587) infliximab and 2% (2/98) adalimumab infusions (no deaths or malignancies). Perianal abscess drainage was less common after anti-TNF initiation (CD): 26% (27/102) before, 7% (3/42) after ($p=0.01$); however pre and post anti-TNF data collection was not over equal time periods.

Conclusion: Anti-TNFs are effective treatments, usually given with thiopurine co-immunosuppression. This study highlights deficiencies in formal documentation of effect and disparity between disease severity scoring tools which need to be addressed to improve ongoing patient care.

Keywords: Paediatric gastroenterology, inflammatory bowel disease, Crohn's disease, ulcerative colitis, biologics (IBD)

What is known:

- Anti-Tumour necrosis Factor (TNF) therapy is a very effective treatment for refractory paediatric Inflammatory bowel disease.
- There are concerns about use of co-immunosuppression and potential increased lymphoma risk.
- Physician Global Assessment (PGA) and Paediatric Crohn's disease activity index (PCDAI) are frequently used measures of disease activity

What is new:

- Formal documentation of response/ remission rates to induction anti-TNF therapy is infrequent.
- The majority of patients in this large cohort are on combination therapy, usually with thiopurines.
- There was disparity between PGA and PCDAI scores; weighted PCDAI is suggested as an alternative.

INTRODUCTION

The Inflammatory Bowel Diseases (IBD), comprising Crohn's disease (CD), ulcerative colitis (UC) and IBD unclassified (IBDU) are increasing in incidence and prevalence, notably in the paediatric population.[1] Paediatric care has been revolutionised in the last decade by the widespread introduction of anti-tumour necrosis factor (anti-TNF) therapy, both infliximab (IFX) and adalimumab (ADA); registration clinical trials have shown these agents to be effective where other therapies have failed.[2,3] Paediatric onset IBD (PIBD) tends to be more extensive at diagnosis and aggressive in behaviour[4,5] and use of anti-TNF therapy is proportionately greater in the paediatric population compared to adults (20% in adolescents vs 8% in adults in one case control study)[6].

IFX and ADA have been licensed for use in PIBD in the UK since 2010 and 2013 respectively; UK survey data has demonstrated effectiveness in treating refractory disease whilst highlighting the potential for serious side effects.[7,8] Scottish data on 132 PIBD patients treated with biologics over a decade show response rates of 87% with IFX (48% remission) and 76% with ADA (35% remission) replicating safety issues, especially serious infection.[9]

The UK IBD audit is a national gastrointestinal audit first commenced in 2006 (reporting in 2008). Reports are available online at www.rcplondon.ac.uk/ibd. Data has previously been published on the outcomes of paediatric and adult patients with UC.[10,11] We aimed to collect data on anti-TNF therapies in UK PIBD practice to assess effectiveness, safety and appropriate use (according to national guidelines) in clinical practice. Unselected, large scale national data will help quantify and categorise adverse events where real life clinical data is lacking.

MATERIALS AND METHODS

Sites (either a single hospital or a represented health board or trust) were eligible to participate in the audit if they prescribe and administer anti-TNF therapies to their patients with IBD, on a voluntary basis. A total of 37 sites participated, including 23 of 25 specialist PIBD sites, representing a broad subset of PIBD patients across the UK. Children with a diagnosis of IBD who were aged 18 years or younger when *newly* started on anti-TNF therapy for IBD from 12/09/11 were eligible for inclusion. Patients already on anti-TNF therapy prior to this date were excluded. Data was collected prospectively and entered into a bespoke web based database, with security maintained through local site codes and the lead clinician for the site authorising local access. All treatment decisions and data entry were at the discretion of the treating physician. Data capture for the results included here ended on 28/02/14.

Demographic details were pseudo-anonymised at the point of data entry and identifiable only to the participating site. IBD disease details were phenotyped according to Montreal criteria for disease location and behaviour.[12] Physician Global Assessment (PGA), Paediatric Crohn's Disease Activity Index (PCDAI) or Paediatric Ulcerative Colitis Activity Index (PUCAI) scores were collected at initial and follow-up treatments, along with details of comorbidities and any surgery.[13,14,15] A full list of all data items collected is available on request.

Acute infusion reactions were as decided by the treating clinical team responsible for the patient; no specific guidance on specific timing was given to teams. Each follow-up treatment relates to an initial submission and records outcome as intention to continue or

stop; response with or without remission using reduction in PCDAI/PUCAI or Harvey Bradshaw Index (HBI).[16] Unlimited numbers of follow-up treatments are permitted and any adverse events recorded. Poor response was used to describe those patients with no or limited response to anti-TNF treatment, which included primary non-responders. Details of IBD related surgery can be added at any time, along with any escalation of treatment at each initial or follow-up treatment. Patient Reported Outcome Measures (PROM) data was collected using the IMPACT-III questionnaire [17–19] at initiation and subsequently.

Some children received treatment with multiple biologics resulting in more initial treatments than patients. Since the number of submissions per patient is variable (e.g. multiple initial or follow-up treatments), the denominators presented vary considerably; results tables should therefore be scrutinised carefully in conjunction with any explanatory notes for accurate interpretation.

Guidance on the use of anti-TNF therapy in the UK comes via the National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC). NICE Technology Appraisals TA187 (CD) and TA329 (UC) recommend Infliximab [and adalimumab] within its licensed indication as an option for "the treatment of people aged 6-17 years with severe active disease who have not adequately responded to conventional therapy (including corticosteroids, immunomodulators and exclusive enteral nutrition [CD]), or who cannot tolerate or have contraindications to conventional therapy".[7,20] Data were collected on disease type and severity as well as previous therapies to assess prescribing against these criteria.

Selected data, including demographics, disease location and response to treatment were compared to data reported in the adult arm of the audit from the same time period, which can be seen at www.rcplondon.ac.uk/ibd.[21]

Data were analysed using SPSS version 19 (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.). Data manipulation was performed using SAS software v9.4 for Windows. Copyright (c) 2002-2012 by SAS Institute Inc., Cary, NC, USA. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA. Chi-squared test and the kappa statistic were used to examine categorical data; the Mann-Whitney U test was used to examine continuous data; Kolmogorov-Smirnov (KS) test was used to analyse PROM data. Kappa statistic is expressed as per the boundaries described by Landis and Koch; range is from 'poor/slight' agreement ($K \leq 0.2$) through 'fair', 'moderate' and 'substantial', to 'almost perfect' agreement (K 0.81-1.00). A p value of <0.05 was considered statistically significant.

ETHICAL CONSIDERATIONS

As an audit of clinical practice, ethical permission was not applied for.

RESULTS

Overview

By 28/02/14, demographic submissions were entered on 817 individual paediatric patients; 156 patients with no initial treatment details entered were excluded leaving 661 patients with 746 initial treatments (some patients were treated with more than one anti-

TNF). Further exclusions resulted in final analysis on 524 patients (429 CD, 76 UC and 19 IBDU) with 562 initial treatments (Figure 1). Patient demographics are shown in table 1. 30 CD, 4 UC and 4 IBDU patients were treated with both anti-TNFs.

Infliximab was the commonest anti-TNF therapy representing 87% (488/562) of initial treatments. 79% (445/562) patients were co-immunosuppressed; 79% (386/488) on IFX (91% thiopurines [351/386], 9% methotrexate [35/386]) and 80% (59/74) on ADA (80% thiopurines [47/59], 20% methotrexate [12/59]). Consent was taken in 99% (559/562), either verbally (46% [257/559]) or written (54% [302/559]). Verbal consent was significantly more common with ADA 51/74 (69%) compared with IFX 206/485 (42%), p=0.00002. In total 51% (223/437) of patients had failed on an immunosuppressant and/or steroids prior to treatment with anti-TNF. 5.2% patients (27/524) had no previous medication or concomitant therapies documented at time of anti-TNF initiation, suggesting a 'top-down' therapy approach.

Crohn's Disease

40% (151/379) of patients starting IFX and 37% (22/60) starting ADA had extensive disease i.e. L3 (ileocolonic) at initiation and 80% (310/388) had upper GI involvement (proximal = L4). The commonest indication for starting therapy was active luminal CD in 78% (355/458); severe perianal CD accounted for 17% (77/458) (Supplemental Digital Content, Table 1, http://links.lww.com/MPG/B43).

Disease severity at initiation of anti-TNF (where documented) was moderate-severe in 91% (156/171, PGA) and 41% (88/217, PCDAI) (table 2).

Cross-tabulation of PCDAI and PGA (grouping mild and remission together for comparison) reveals a Kappa statistic (K) of 0.28 (SE=0.055, $p<0.001$) indicating only

'fair agreement'. PCDAI was less frequently recorded than PUCAI; 51% (217/429) PCDAI compared to 64% (53/76) PUCAI, p=0.02.

99% (347/349) of initial IFX was given at 5mg/kg i.e. standard dosing. 71% (45/63) ADA was given at 80mg/40mg whilst 25% (16/63) was given at 160mg/80mg induction dose. Outcomes of treatment are shown in table 3; of note, planned withdrawal following effective treatment occurred in just 21% (9/42) of IFX cessation and no cases with ADA.

Ulcerative Colitis

The majority of patients had extensive disease (E3) at initiation (table 1). Chronic refractory UC was the commonest indication (59% [47/79] treatments) but 39% (31/79) were for acute severe UC (Supplemental Digital Content, Table 1, http://links.lww.com/MPG/B43). All IFX infusions were prescribed at 5mg/kg and 86% (6/7) of ADA given at 80mg/40mg induction dose.

Disease severity was moderate-severe in 92% (35/38, PGA) compared to 85% (45/53, PUCAI). Median PUCAI score at initiation was 55 (IQR 40, 70), (table 2). Cross-tabulation had a Kappa statistic of 0.58 indicating 'moderate' agreement (0.41-0.60) between PGA and PUCAI.[22]

There was 97% follow-up for ongoing IFX treatments (168/174), median 94 days (IQR 21, 215) and 83% (5/6) for ongoing ADA treatments, median 130 days (IQR 114, 304). 12% treatments were stopped (21/173), with poor response or loss of response equally accounting for 76% (16/21). Where PGA was documented, disease severity (n=100) improved in most at follow-up (n=38) (table 2).

IBD Unclassified

95% (20/21) of IBDU patients had extensive disease (E3) at initiation. Acute severe and chronic refractory IBDU accounted for an equal proportion of treatments. There was 97% follow-up for ongoing anti-TNF at a median of 44 days (IQR 14, 98) for IFX. 16% treatments were stopped (n=5); poor response (2/5), adverse effects (2/5), loss of response (1/5). Disease severity where recorded at follow-up was mild in 10%, moderate in 76% and severe in 14% (n=21), compared to 0% mild, 22% moderate and 78% severe at initiation (n=9).

Disease severity was moderate-severe in 100% (9/9) IBDU at initiation by PGA, where documented, compared with 62% (5/8) by PUCAI.

Response and remission

Response to induction was infrequently formally recorded; 17% (89/524) all IBD (CD 74/429, UC 12/76, IBDU 3/19). 75% (67/89) patients responded (fall in PCDAI ≥15, fall in PUCAI ≥20 or remission) at 10-14 week follow-up (CD 78% [58/74], UC/IBDU 60% [9/15]); 60% (56/93) achieved remission (CD 64% [50/78], PCDAI score ≤10 and UC/IBDU 40% [6/15], PUCAI <10).

Surgery

105 paediatric patients had surgery involving 156 IBD-related surgical procedures. There was no significant difference between surgery in the 6 months pre and post initiating biologic; 7% (36/524) pre and 5% (27/524) post (p= 0.30). 87% (136/156) procedures were in CD patients, 8% (13/156) in UC patients and 5% (7/156) in patients with IBDU. The commonest surgical procedure in UC/ IBDU was sub-total colectomy with ileostomy. The commonest procedures (by disease type) are detailed in Supplemental Digital Content, Table 2, http://links.lww.com/MPG/B44. The commonest procedure

overall was examination under anaesthetic (EUA) of fistula, 24% (40/166) of all surgical procedures, 27% (39/144) CD procedures. Drainage of perianal abscess was significantly less common in CD after anti-TNF than before 28% (27/96) vs. 8% (3/39) (p=0.01). However the time period of data collection was not equal pre and post anti-TNF and was variable from patient to patient. In total, 16% (12/74) of UC patients went on to have colectomy (Supplemental Digital Content, Table 2, http://links.lww.com/MPG/B44).

Safety data

There were 2287 infusions and 301.96 years of patient follow-up (n=385); median 0.65 (IQR 0.27-1.19).

2% (10/488) of all initial IFX infusions and 1% of all follow-up IFX infusions (23/1587) reported an acute reaction. There were no acute reactions with any ADA treatment (0/173). 3% (49/1587) of IFX and 2% (2/98) ADA infusions reported an adverse event, most commonly infection (Supplemental Digital Content, Table 3, http://links.lww.com/MPG/B45), although type and severity of infection was not specified. 10% of CD patients (32/316) experienced at least one adverse event over the course of their treatment. No malignancies or mortality were reported.

Pre-treatment Screening

Tuberculosis (TB) screening was carried out: 97% (478/493) had at least 1 test for TB ; 88% (433/492) patients had a chest x-ray, 47% (224/481) a gamma interferon TB test and 3% (15/469) a Mantoux test. 71% (343/485) patients were screened for Varicella immunity; 46% (221/482) for Hepatitis B infection and 37% (176/480) for Hepatitis C; 12% (57/476) were screened for HIV infection.

Comparison to adult data

Comparison was made to data from the adult biologic audit which ran over the same time period. There was a male preponderance in the paediatric cohort, with more extensive disease distribution and shorter time from diagnosis to anti-TNF initiation. Response and remission rates were comparable but more children were co-immunosuppressed at the time of starting anti-TNF (Supplemental Digital Content, Table 4, http://links.lww.com/MPG/B46).

Patient Reported Outcome Measures (PROM)

19% (98/524) had IMPACT-III scores recorded at baseline with 33% (32/98) with a repeat at follow-up (Supplemental Digital Content, Table 5, http://links.lww.com/MPG/B47). The median (IQR) baseline score for IBD was 110.5 (91.0, 129.0) and at follow-up 113.5 (82.0, 141.0) and for CD (n=78) 110.5 (92.0, 130.0) and 128.5 (85.0, 147.5) respectively. When considering patients with both baseline and follow-up scores (CD n=25, all IBD n=32) CD; 98.0 (87.0, 136.0) to 109.0 (72.0, 156.0), and 'all IBD'; 103.5 (87.0, 131.5) to 101.0 (68.0, 147.5) (ns for both). It should be noted that a change of 10.8 or more is considered a significant change by the IMPACT-III design team.[23]

DISCUSSION

This large cohort of paediatric patients receiving anti-TNF therapy over a 2.46 year period gives a snapshot of use in real life clinical practice for PIBD across the UK. Overall response and remission rates are good (75% patients responding and 60% achieving remission), but one of the key outcomes is that formal documentation of this is

infrequently done (17% patients). This is despite patients going on to receive maintenance therapy after their induction course. We highlight the need for formal post-induction assessment of response to determine the need for on-going treatment and suggest a validated scoring system as the best method. Failure to do this formally is highly concerning; patients may continue to receive treatment that is failing or not have appropriate investigations performed e.g. trough level determination.

Complete accrual of all anti-TNF use, effectiveness and safety has been published in a nationwide Scottish PIBD registry study, but this only represents 8% of the UK paediatric population.[9] Lower remission rates of 48% and 36% for IFX and ADA respectively were reported here but the period studied was longer 2000 – 2010, perhaps reflecting early use of anti-TNF when current standard practice, such as maintenance rather than episodic treatment and dose optimisation, was not in place.[9] A previous UK survey of adalimumab for paediatric CD reported a remission rate of 61% at follow-up[8] and the RESEAT study a 65-71% clinical response rate at 3-12 months of ADA therapy in paediatric CD,[24] which are comparable despite our low documentation rate.

There is a clear discrepancy between PGA and PCDAI scores. Documentation of PCDAI at follow-up was low, as in previous studies, thought potentially due in part to the inclusion of items that are less readily obtained such as height velocity, perianal examination and laboratory indices.[15,25] Formal documentation of such data can be seen as a low priority in busy clinical practice. PCDAI was less frequently recorded than PUCAI here, which may support the theory that a simpler score is better used. Recently, the weighted PCDAI (wPCDAI) has been proposed as an alternative measure to the PCDAI and shown to have validity despite the exclusion of haematocrit, abdominal

examination and height velocity as parameters.[26] Replacing PCDAI with wPCDAI in subsequent rounds of the audit may encourage increased completion and thereby facilitate more objective clinical assessment and aid decision making. An app to allow easy calculation of wPCDAI and documentation was produced as a result of this study. The PUCAI appeared to have better correlation with PGA than PCDAI, in keeping with other studies specifically designed to test this which show excellent agreement.[15]

There was a significant reduction in the need for drainage of perianal abscess after initiation with anti-TNF. We note that time periods pre and post initiation were not equal or defined, limiting the strength of any conclusions drawn from this, but we know that perianal disease is recognised as a debilitating CD phenotype and anti-TNFs have been shown to be an effective treatment in large studies.[27] The rate of colectomy in UC patients at 16% is in keeping with adult studies[28,29], rate of colectomy post anti-TNF in IBDU patients is notable at 21% but numbers are small (4/19).

Although the follow-up period is relatively short (max 2.46 years), the large number of patients allows us some confidence in the short term safety profile of the anti-TNF therapies, as 2287 infusions and 302 years of patient follow-up are represented. Infection was the commonest adverse event, in keeping with other published studies[30,9] and whilst risks are minimised where possible, total prevention is not achievable. Despite safety concerns about the use of combination therapy and lymphoma risk, it is interesting to note that the majority of patients in this cohort were on combination therapy. Recently published registry data from a very large cohort of paediatric patients (some from the UK) have shown no increased risk of malignancy during longer term follow up,

supporting the good safety profile of infliximab,[31] as with previous anti-TNF safety data.[32]

Screening practice is variable; exclusion of TB infection is an obligatory part of guidelines so there remains room for improvement in the final unscreened 3%.[33,34] The risk of hepatitis B reactivation is well known but despite this less than half of patients were screened, highlighting a need to improve on this.

The shortened time from diagnosis to starting anti-TNF in the paediatric population compared to adults is striking; it suggests aggressive progression of disease and rapid cycling though medical therapeutic options, although potentially reflects poorer tolerance of standard treatments and the context of aiming for steroid free remission as quickly as possible to minimise impact on growth, puberty and education.

It is difficult to draw any meaningful conclusion regarding impact on quality of life (QoL) due to the small numbers of documented PROMs. Completion in subsequent audit rounds should be promoted as improvement in QoL is an important outcome and cannot be assumed from other markers of response. Of note, significant improvement in QoL using IMPACT 3 in paediatric patients has been recently documented in a formal clinical study.[35]

The main limitation of this study is the variability in completeness of data capture, reflected in the changing denominator for different categories of data. This audit relies on clinical centres finding time to enter patient data and it is often only possible for them to supply the minimum data set. By comparison it is a major undertaking to capture all biological usage and outcomes in a PIBD population.[9] Follow-up is relatively short therefore the ongoing medical and surgical course of those who do not respond is

unknown. Its strength however lies in the nationwide collaborative nature of the project and relatively large numbers represented, with over 90% of specialist sites participating and the 'real-world' clinical data which should mean conclusions that can be drawn are broadly generalisable to the PIBD population. Addressing the major issue of poor documentation of post induction response is likely to result in a significant improvement in the clinical care PIBD patients. The large number of treatments in routine clinical use support anti-TNF therapy as safe and effective in paediatric IBD with the majority of patients achieving response or remission and just 2% of initial infusions and 1% of follow-up infusions associated with acute adverse reactions.

Future audit is increasingly important with bio-similars now licensed for use in PIBD in the UK; generating comparative clinical data on their efficacy and safety profile is essential to evaluate their use, given the current lack of any published evidence in IBD. Ongoing national collaboration would be the best way to achieve this quickly and meaningfully.

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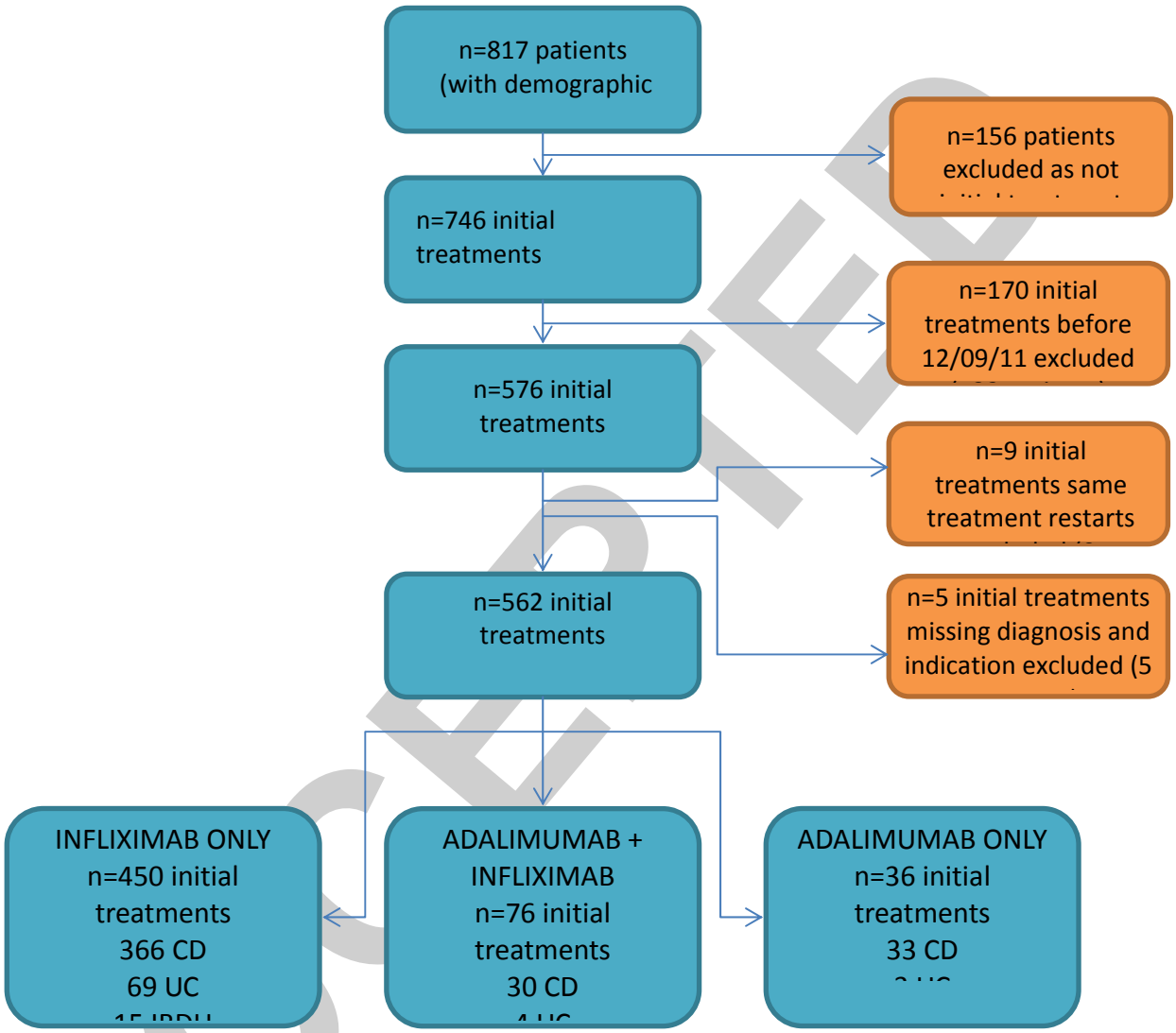

Fig 1. Patient flow chart. CD, Crohn's Disease; UC, Ulcerative Colitis; IBDU Inflammatory Bowel Disease Unclassified.

Summary table	CD n=429	UC n=76	IBDU n=19	All IBD n=524
General patient characteristics				
Gender: Male	62% (267/429)	58% (44/76)	53% (10/19)	61% (321/524)
Age at diagnosis, years, median (IQR)	n=411 12.0 (9.4, 13.8)	n=74 12.3 (9.5, 14.2)	n=17 11.7 (8.9, 12.8)	n=502 12.0 (9.4, 13.9)
Age at initial treatment, years, median (IQR)	n=427 14.2 (13.5, 15.7)	n=76 13.1 (11.7, 15.4)	n=19 13.5 (11.0, 14.8)	n=522 14.1 (12.3, 15.7)
Time from diagnosis to biologic, years, median (IQR)	n=411 1.43 (0.65, 3)	n=74 1.08 (0.3, 2.23)	n=17 0.82 (0.06, 3.5)	n=502 1.36 (0.61, 2.92)
Commonest disease distribution at decision to initiate treatment (by Montreal classification)				
Colonic (L2)	40% (164/410)	-	-	
Ileocolonic (L3)	41% (166/410)	-	-	
Any gut proximal to TI (L4)	79% (288/364)	-	-	
Perianal involvement = Yes	54% (146/270)	-	-	
Extensive colitis (E3)	-	74% (54/73)	94% (16/17)	78% (70/90)

Table 1: Overview of demographics and disease details by IBD type. IQR, Inter Quartile Range; PCDAI, Paediatric Crohn's Disease Activity Index; PUCAI, Paediatric Ulcerative Colitis Activity Index

Disease severity at initial treatment (per patient)	CD n=429	UC n=76	IBDU n=19	All IBD n=524
PGA	n=171	n=38	n=9	n=218
Mild	9% (15/171)	8% (3/38)	0% (0/9)	8% (18/218)
Moderate	55% (94/171)	45% (17/38)	22% (2/9)	52% (113/218)
Severe	36% (62/171)	47% (18/38)	78% (7/9)	40% (87/218)
PCDAI	n=217	-	-	n=217
median (IQR)	29 (20, 38)	-	-	29 (20, 38)
≤10 (Remission)	12% (26/217)	-	-	-
11-30 (Mild)	47% (103/217)	-	-	-
31-37.5(Moderate)	17% (36/217)	-	-	-
≥40 (Severe)	24% (52/217)	-	-	
PUCAI	-	n=53	n=8	n=61
median (IQR)	-	55 (40, 70)	43 (15, 58)	55 (39, 66)
0-9 (Remission)	-	4% (2/53)	25% (2/8)	7% (4/61)
10-34 (Mild)	-	11% (6/53)	13% (1/8)	11% (7/61)
35-64 (Moderate)	-	42% (22/53)	38% (3/8)	41% (25/61)
65-85 (Severe)		43% (23/53)	25% (2/8)	41% (25/61)

Table 2: Disease severity at initial treatment. PGA, Physician Global Assessment; IQR, Inter Quartile Range; PCDAI, Paediatric Crohn's Disease Activity Index; PUCAI, Paediatric Ulcerative Colitis Activity Index.

Crohn's Disease Follow-up anti-TNFα treatment	Infliximab (Frequency %) n=1414	Adalimumab (Frequency %) n=97
Follow-up outcome		
Seen for follow-up	98% (1389/1414)	91% (88/97)
Transitioned to adult care	2% (23/1414)	8% (8/97)
Transferred to another service	0.1% (2/1414)	1% (1/97)
Median days from initial dose to follow-up (IQR)	167 (46, 350)	81 (35, 232)
Current plan		
Continue treatment	97% (1346/1388)	91% (84/92)
Stop treatment	3% (42/1388)	9% (8/92)
Reason for stopping (if treatment stopped)		
Treatment effective and discontinued	21% (9/42)	0% (0/8)
Loss of response	17% (7/42)	38% (3/8)
Poor response	29% (12/42)	50% (4/8)
Side effects / adverse events	14% (6/42)	0% (0/8)
Other	19% (8/42)	13% (1/8)
Disease severity (PGA)		
Mild	69% (500/726)	26% (17/65)
Moderate	26% (186/726)	51% (33/65)
Severe	6% (40/726)	23% (15/65)

Table 3: Outcome at follow-up in Crohn's Disease; IQR, Inter Quartile Range; PGA, Physician Global Assessment