ABSTRACTS

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Oral Presentations

O-001

Modified Exclusive Enteral Nutrition with the Crohn Disease Exclusion Diet is effective for Induction and Maintenance of Remission in children with Crohn Disease; the DIETOMICS-CD trial

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Objectives and Study: Exclusive enteral Nutrition (EEN) is considered a first line therapy for children with active Crohn disease (CD). CD Exclusion Diet (CDED)+Partial Enteral Nutrition (PEN) is effective for induction of remission in mild-moderate CD at weeks 6 and 12, with better tolerance than EEN. To expand potential impacts of CDED, we assessed whether a 2-week course of CDED, followed by CDED+PEN is superior to 8 weeks of EEN in sustaining clinical remission at week 14, longer term outcomes of CDED (up to 24 weeks), and utility in a broader spectrum of patients (mild to severe).

Methods: This open-label, international, multicenter, randomized-controlled trial compared 2 weeks of EEN (Modulen, Nestle Health Science) followed by 3 phases of the CDED+PEN (phase 1: weeks 3-8; phase 2: weeks 9-14; phase 3: weeks 15-24) to 8 weeks of EEN, followed by PEN (25%) with free diet up to week 24. Children (aged 8-21) with recently diagnosed CD (<3 years), mild-severe disease [paediatric CD activity index (PCDAI) 15-47.5], and active inflammation [elevated C-reactive protein (CRP) or fecal calprotectin (FCP)] were included. Predominantly distal colonic, extraintestinal, and perianal disease were excluded and only stable immunomodulator (IM) treatment was allowed. Naïve patients were allowed to start an IM from week 4. The primary outcome was steroid-free sustained clinical remission at week 14.

Results: Fifty-five of 63 eligible patients were randomized and included in the final intention to treat analysis (target recruitment failed due to COVID pandemic); 29 were allocated to group 1 (CDED+PEN) and 26 to group 2 (EEN); mean age: 12.7±2.4. Steroids-free sustained remission at week 14 was obtained in 20/29 (69%) in group 1 and 16/26 (61.5%) in group 2; 16/29 (55%) in group 1 and 9/26 (34%) in group 2 maintained clinical remission at week 14.

Median CRP improved in group 1 from 32 mg/L [6-69] at baseline to 5 [2-16] at week 8 and 3 [2-10.1] at week 14 (p<0.001 for both), and in group 2 from 10.35 mg/L [5-33] at baseline to 3.75 [0-11.8] at week 24 in group 2 (p<0.005 for all). Median FCP improved in group 1 from 32 mg/L [6-69] at baseline to 5 [2-16] at week 8 and 3 [2-10.1] at week 14 (p<0.001 for both), and in group 2 from 10.35 mg/L [5-33] at baseline to 3.75 [0-11.8] at week 24 in group 2 (p<0.005 for all). Median PCDAI declined from 32.5 [20-36.2] (baseline) to 2.5 [0-5.6] at week 8, 1.2 [0-5.6] at week 14, and 1.2 [0-10] at week 24 in group 1 (p=0.012), and from 22.5 [20-29.3] to 0 [0-4.3] at week 8, 0 [0-2.5] at week 14, and 3.75 [0-11.8] at week 24 in group 2 (p=0.006). Median FCP declined in group 1 from 1946 [862-3304] to 802 [196-1312] at week 8 and 241 [82-1175] at week 14 (p<0.01 for
both), and in group 2 from 1615 [605-2692] at baseline to 436 [252-1389] at week 8, which then in-
creased to 731 [349-1305] at week 14 (p<0.01 for both). At week 14, 12/22 (54%) received IM from
group 1 and 15/16 (93%) from group 2; p = 0.009.

Conclusions: Two weeks of EEN followed by CDED&PEN and EEN were successful in induction of
clinical and biochemical remission in mild-severe paediatric CD, and most CDED+PEN patients-main-
tained remission to 24 weeks. Sustained clinical remission at week 14 was similar; however, calpro-
tectin rebounded at week 14 in EEN group but not in CDED+PEN despite higher IM use in the EEN
Group, suggesting that CDED might prevents diet-induced inflammation.

Conflict of Interest:

1. R.S.B: Speaker fees, Consulting and Advisory board - Nestlé Health Science
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Diet-Omics characterization of new onset treatment naive Crohn Disease identifies factors that may contribute to disease pathogenesis

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Objective and Study: Crohn Disease (CD) prevalence is rising worldwide. As altered genetics are improbable, this phenomenon likely relates to modern era environmental and dietary change, linked to the gut microbial composition. We used dietary and Multi-OMIC characterization to define host and microbial factors at CD diagnosis.

Methods: Clinical data, biomarkers (CRP, fecal calprotectin) computerized food frequency questionnaire (FFQ), and Multi-OMICs analyses including serum metabolomics, mucosal terminal ileum (TI) transcriptomics, and fecal and mucosal biopsy samples for 16S microbial amplicon sequencing.

Results: 25 newly-diagnosed CD and 33 controls (50% males) were included, and gender, age, and BMI did not differ between groups, but CRP (p=0.001) and calprotectin (p=E-10) were significantly higher in CD. FFQ results showed that compared to controls, pre-diagnosis CD patients consumed significantly more added sugar (g/day), starch (g/day) nitrite (mg/day), and significantly less vitamin K, D, and vegetables and olive oil servings per day (Fig 1A). Microbial analyses highlighted significant differences (FDR<0.1) in microbial amplicon sequence variants (ASVs) abundance between luminal (stool) and mucosal (biopsies) samples (73 ASVs) and between CD and Controls samples (82 ASVs). Biopsy vs. stool samples were enriched for Veillonella, Fusobacterium, Neisseria, and Ruminococcus gnavus. CD showed higher abundance of Enterobacteriaceae and Ruminococcus gnavus with reduction of several Ruminococcaceae and Lachnospiraceae taxa (Fig. 1B). Ileal transcriptomics highlighted 8 specific gene co-expression modules with specific functional enrichments for induction of innate epithelial pro-inflammatory genes (DUOX2), induction of OSM/cytokines linked with extra cellular matrix (ECM) signal, and reduction in epithelial metabolic pathways and epithelial barrier functions. Those transcriptomics co-expression gene modules showed significant correlation with dietary factors with signals that may contrast (protect) or exacerbate (worsen) mucosal host disease signals; higher coffee and water consumption showed negative associations with OSM/cytokines/ECM, while higher fat consumption was positively associated with the module that contained calprotectin (S100A8/9) genes and TLR2/8. Serum metabolomics highlighted significant variations (FDR<0.25) inLinoleic acid, aK, Tryptophan, nicotinamide, Docosahexaenoic acid, oxalate, and GABA between CD and controls. Vegetables consumption was positively associated with oxalate degrading Oxalobacter (Fig. 1C), and both were decreased in CD, together with higher serum oxalate. Associations between diet and TI transcriptomics indicated that B12, tryptophan and riboflavin consumptions were neg. associated with the bile acid transporter SLC10A2 in the TI (Fig. 1D). Associations between gut microbiome and serum metabolomics showed that oxalate was pos. associated with Erysipelotrichaceae taxa and GABA was neg. linked with Oscillospira (Fig. 1E) taxa which was previously linked with neurologic conditions like Autism and Parkinson’s.

Conclusions: FFQ identifies difference in diet at the onset of CD that may contribute to pathogenesis. Integration between dietary and OMICs layers disclosed original correlations that may guide novel mechanisms to redirect disease signals.
Fig. 1 | Integration between dietary and OMICs layers disclosed intriguing correlation between gut microbiome, serum metabolomics, and food frequency consumption. This prospective cohort included 25 CD and 33 controls. Subjects answered computerized food frequency questionnaire (FFQ) and underwent diagnostic endoscopy. Mucosal biopsies, serum, and stool samples were obtained. A. FFQ highlighted significant differences (*p<0.05) between groups at the time of diagnosis. CD consumed significantly more added sugar (g/day), starch (g/day) nitrite (mg/day), and significantly less vitamin K, D, vegetables, and olive oil (serving/day). B. Heatmap showing 82 significant ASVs that differed between CD and controls. Sample source is indicated above the heatmap, and diagnosis is noted under the heatmap. Bacterial Amplicon Sequence Variant (ASV) in rows and different subjects in columns. C. Significant correlation between dietary intake and gut microbiome whereby vegetables consumption was positively associated with oxalate degrading Oxalobacter. D. Significant correlation between dietary intake and TI transcriptomics with B12, tryptophan, and riboflavin consumptions negatively associated with the bile acid transporter SLC10A2 in the TI. E. Significant correlation between gut microbiome and serum metabolomics whereby oxalate showed positive association with Erysipelotrichaceae_toxa and GABA (higher in CD) was neg. linked with Oseilliospira, which was previously linked with neurologic conditions like Autism and Parkinson’s (FDR=0.25).
**O-003**

**Colorectal Cancer in Childhood-Onset Inflammatory Bowel Disease: a Scandinavian Register-based Cohort Study, 1969-2017**


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**Objectives and Study:** Colorectal cancer (CRC) surveillance programs for patients with inflammatory bowel disease (IBD) are based on phenotype, but do not consider age of IBD onset. It is unknown whether CRC surveillance of childhood-onset IBD should differ from that of adult-onset IBD.

**Methods:** Patients with incident childhood-onset IBD (<18 years) 1969-2017 were identified using colorectal biopsy data and Danish and Swedish National Patient Registers. The patients were matched to IBD-free reference individuals by sex, age, place of residence, and year of IBD diagnosis. We linked data to Cancer and Causes of Death Registers and used Cox regression to estimate risks of incident CRC and death from CRC.

**Results:**

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Crohn's Disease/Reference</th>
<th>Ulcerative Colitis/Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>N total</td>
<td>6037/69,148</td>
<td>8518/84,866</td>
</tr>
<tr>
<td>N events</td>
<td>25/43</td>
<td>113/95</td>
</tr>
<tr>
<td>Incidence proportion (%)</td>
<td>0.36/0.06</td>
<td>1.33/0.05</td>
</tr>
<tr>
<td>Person years</td>
<td>96,204/101,072</td>
<td>11,839/129,258</td>
</tr>
<tr>
<td>Incidence rate (95% CI) per 100,000 person years</td>
<td>0.26 (0.18 - 0.34) / 0.04 (0.01 - 0.06)</td>
<td>1.00 (0.88 - 1.20) / 0.04 (0.01 - 0.05)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hazard ratios</th>
<th>Crohn's Disease vs reference</th>
<th>Ulcerative Colitis vs reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>N cancer diagnoses in IBD/1000 person years, HR (95% CI)</td>
<td>5/96, 0.46 (95% CI: 0.95-10.6)</td>
<td>113/113, 52.5 (23.0-45.9)</td>
</tr>
</tbody>
</table>

**Conclusions:** Because of the scarcity of pediatric data with large enough sample size and long enough follow-up, current endoscopic surveillance programs are mainly based on adult data, all recommend varied colonoscopy intervals according to presence of risk factors (e.g., total colitis in UC, colonic involvement in CD and occurrence of primary sclerosing cholangitis) and do not take age of...
IBD-onset into account. The results from this study show that the relative risk of CRC is very high in both childhood-onset CD and UC, and not only for those with the aforementioned risk factors. The absolute risk of CRC cancer diagnosis was also substantial (1.33% in UC and 0.36% in CD) for a population of median age 27 years at end of follow-up. We think it is fair to suggest that childhood-onset IBD should be considered an additional risk factor when implementing colorectal cancer surveillance programs in IBD.

Conflict of Interest: Å H Everhov have worked on projects at Karolinska Institutet and SWIBREG partly financed by grants from Ferring and Jansen. J F Ludvigsson coordinates a study on behalf of the Swedish IBD quality register (SWIBREG), which has received funding from Jansen corporation. O Olén has been PI on projects at Karolinska Institutet, partly financed by investigator-initiated grants from Janssen and Ferring, and Karolinska Institutet has received fees for lectures and participation on advisory boards from Janssen, Ferring, Takeda, and Pfizer. O Olén also reports a grant from Pfizer in the context of a national safety monitoring program. J Askling acts or has acted PI in agreements between Karolinska Institutet and the following entities, mainly regarding safety monitoring of Rheumatology immunomodulators: Abbvie, AstraZeneca, BMS, Eli Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB. J Halfvarson served as speaker and/or advisory board member for AbbVie, Celgene, Celltrion, Dr. Falk Pharma and the Falk Foundation, Ferring, Hospira, Janssen, MEDA, Medivir, MSD, Novartis, Olink Proteomics, Pfizer, Prometheus Laboratories, Sandoz, Shire, Takeda, Thermo Fisher Scientific, Tillotts Pharma, Vifor Pharma, UCB and received grant support from Janssen, MSD, and Takeda. H T Sørensen, R Erichsen, and L Pedersen report that the Department of Clinical Epidemiology, Aarhus University Hospital, receives funding for other studies from companies in the form of research grants to (and administered by) Aarhus University. None of these studies have any relation to the present study.
O-004

Long-term outcomes in paediatric-onset PSC-IBD: A retrospective Canadian cohort study

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Objectives and Study: PSC represents a leading cause of morbidity and mortality in IBD patients. However, the long-term data on colonic and hepatobiliary outcomes necessary to adequately counsel families of children with this unique phenotype, PSC-IBD, are currently lacking. The Sclerosing Cholangitis Outcomes in Pediatrics (SCOPE) index (comprising total bilirubin, albumin, platelet count, GGT and cholangiography) was developed to assist hepatobiliary outcome prognostication. We aimed 1) to characterise intermediate and long-term outcomes in paediatric PSC/PSC-IBD and prognostic factors, and 2) compare outcomes in paediatric- vs. adult-onset disease.

Methods: We performed a two-centre retrospective study including the largest paediatric and adult PSC clinics in Toronto (SickKids and Toronto General Hospital (TGH)). Children aged <18 y diagnosed between 2000-2018, at either centre, were compared with patients diagnosed as adults. Primary outcomes assessed were time from diagnosis to liver transplant or colectomy. Secondary outcomes included time to any hepatobiliary complications, biologic therapy, cancer, and death. Outcome differences between groups were assessed using chi-square and MWU or t-test, as appropriate. Predictive modelling using Cox proportional hazard regression was performed to ascertain phenotypic, laboratory and imaging predictors of long-term outcomes, both individually and as the composite SCOPE index.

Results: 95 paediatric-onset PSC patients (median age at diagnosis 14.1y (IQR 10.8 - 16.2), follow-up time 8.4 y (IQR 4.8 - 13.3)) and 393 adult-onset PSC patients (median age at diagnosis 36.6 y (IQR 26.7 – 49.0), follow-up 9.6 y (6.4 – 13.3)) were included. Large duct PSC was present in 89.5% of paediatric patients and 92.1% of adult patients (p=0.410), with 87.9% and 75.6% having PSC-IBD in paediatric and adult patients respectively (p=0.074). Paediatric-onset PSC, compared to adult-onset disease, had significantly more autoimmune sclerosing cholangitis (ASC), 27.4% versus 10.2% respectively (p<0.001). Paediatric-onset patients progressed to transplant at a significantly faster rate than those with adult-onset PSC, as shown in Figure 1. By 10 years of disease, 3.2% of paediatric-onset PSC-IBD had undergone colectomy compared to 14.7% of adult-onset PSC-IBD (p=0.003), the primary difference being due to increased rates of dysplasia and adenocarcinoma with age. Colorectal dysplasia or carcinoma occurred in 8.5% of adults compared to 2.5% of children followed out to 10 years (p=0.052). Amongst those with paediatric-onset disease, concomitant IBD was not predictive of significantly improved survival with native liver (HR 0.74, 95%CI: 0.21 -2.59) or event free survival (HR 0.87, 95%CI 0.63 - 1.21) compared to PSC alone. Baseline SCOPE risk score was predictive of liver transplant and death in both paediatric-onset and adult-onset disease, p=0.0346 and p=0.0095 respectively.
Conclusions: PSC has a chronic, progressive course in children with shorter survival with native liver compared to adult-onset disease. By 10 years of PSC-IBD, significantly fewer children than adults had undergone colectomy, with some evidence that this difference is driven by colorectal dysplasia/carcinoma rates. For the first time, we have demonstrated that the Paediatric SCOPE index accurately predicts long term outcomes in adult-onset disease also.
Serum proteomic analysis reveals novel biomarkers associated with disease activity in pediatric patients with Crohn’s disease

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Objectives and Study: Although Crohn’s disease (CD) is associated with a marked hyper-inflammatory response, identifying serum biomarkers associated with disease activity and outcomes is considered challenging, given lack of sensitivity of different assays. Our aim was to identify novel serum markers of disease activity in pediatric patients with CD, using Olink, a novel technology based on proximity extension assay, enabling detection of minute amounts of proteins.

Methods: Serum samples were obtained from pediatric patients with CD at the time of diagnosis and following induction therapy, and from control subjects, consisting of pediatric patients with normal endoscopic procedures, without past or present history of an immune-mediated disorder (e.g. celiac, diabetes). Serums were subjected to Olink (two panels used, consisting of 184 proteins), and analysis was performed on a Normalized Protein eXpression file by supervised, multivariate, principal component analysis and verification by univariate ANOVA with Benjamini-Hochberg and post-hoc Tukey analysis.

Results: Eighty-eight serum samples were collected: 30 from control subjects and 58 from 32 patients with CD (24 of them pre- and post-induction therapy). The median age of patients in the control and CD groups was 13.9 years (IQR 11.1-16.6) and 14.6 years (IQR 12.2-16.9), respectively (P=0.32). Twenty-four patients with CD were treated with anti-TNFα agents and 8 with EEN. The median pediatric Crohn’s Disease Activity Index (PCDAI) decreased from 35 (22.5-42.5) to 5 (0-12.5, P<0.001) following induction therapy. We identified 72 proteins that significantly differed between patients and controls, and many of them were associated with CRP or ESR levels. String analysis identified several important nodes linking different proteins, including MMPs, MPO, EGFR and TNFRSF1A. Many proteins, such as resistin and different MMPs, showed a strong positive correlation with disease activity, based on PCDAI, while others, such as EGFR, showed a negative correlation. Several novel markers were identified, such as LRIG1, an intestinal stem cell marker, that was highly correlated with disease activity among patients with CD.

Conclusions: We identified novel serum markers that are associated with disease activity in pediatric patients with CD. These findings should be validated in future studies, and be complemented with expression and functional studies to define their role in mediating intestinal immune responses.
Transabdominal bowel ultrasound and clinical outcomes over one year in children with newly diagnosed Crohn’s disease


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Objectives and Study: Transabdominal bowel ultrasound (TABUS) is an emerging non-invasive tool for monitoring inflammatory bowel disease (IBD). Its use is particularly increasing in pediatric IBD, given the need for general anesthesia when undergoing endoscopy. The assessment of TABUS in pediatric IBD has been limited to small numbers of patients, with no long-term follow-up. The objective of this study was therefore to describe TABUS findings and assess its clinical utility in pediatric patients with Crohn’s disease up to a year post-diagnosis.

Methods: Pediatric patients (0-18 years old) with suspected IBD were prospectively enrolled through the Edmonton Pediatric IBD Clinic in Alberta, Canada. Those with Crohn’s disease were included and were assessed for a minimum of 6 months, up to 12 months. Patients underwent TABUS, endoscopy, blood work, and fecal calprotectin (FCP). The weighted pediatric Crohn’s disease activity index (wPCDAI), simple endoscopic score for Crohn’s disease (SES-CD; modified to exclude rectum), and the simple ultrasound score for Crohn’s disease (SUS-CD; modified to exclude rectum) were used. Remission was defined as meeting all of the following criteria: FCP<250mg/kg, CRP<4mg/L, ESR<10mm/hr, wPCDAI<12, and no surgery.

Results: Forty-seven patients (68% male), median age 12.5 years (range 6-17), were followed for 6 months. Thirty-six (77%) were followed up to 12 months. Median TABUS bowel wall thickness (BWT) and SUS-CD scores improved in all bowel segments over time. SUS-CD total scores significantly correlated with baseline (rho=0.37) and repeat SES-CD (rho=0.69 at 6 months; rho=0.71 at 12 months) (p<0.05). There were also significant correlations between SUS-CD total scores and the following clinical and biochemical markers: baseline wPCDAI (rho=0.35), ESR (rho=0.52), CRP (rho=0.44); three-month wPCDAI (rho=0.30), ESR (rho=0.49), CRP (rho=0.48); six-month wPCDAI (rho=0.57), ESR (rho=0.40), CRP (rho=0.44), FCP (rho=0.48); and twelve-month wPCDAI (rho=0.47), ESR (rho=0.48), FCP (rho=0.51). Patients who were in remission by 6 months (n=18/47), compared to those who were not, had no differences in baseline endoscopy or TABUS, but had significantly lower SUS-CD total scores by 3-months (1, IQR 0-2 vs. 2.5, IQR 1-4) and 6-months (0, IQR 0-1 vs. 2, IQR 0-2.8) (p<0.05). The median SUS-CD total score improved at each time point for patients who never needed biologic therapy (n=10) and patients who had biologic induction therapy (n=16) (Figure 1). An interval worsening median SUS-CD total score from 1 to 3 months was identified in those who needed subsequent escalation of maintenance therapy to biologics (n=10) (Figure 1). Seven patients had surgery (n=7/7 ileoecal, n=2/7 jejunal resection). Patients who needed surgery had worse changes in the ileum on baseline TABUS (median BWT 8.9 vs. 3.8 mm; SUS-CD doppler 2 vs. 1; p<0.05). All 7 patients had complex TI disease (n=6 strictures, n=1 long-segment disease >25cm) and proximal small bowel disease (n=2/2) on TABUS. Endoscopy missed 1 of the strictures seen on TABUS.
Conclusions: TABUS findings sustained significant correlations with clinical, biochemical, and endoscopic markers of disease activity over the first year post-diagnosis in pediatric patients with Crohn’s disease. The baseline TABUS BWT, doppler, and presence of complex disease can help predict future surgical resection. The three-month TABUS is particularly important in helping identify those who may need escalation of therapy.
Analysis of the intergenerational epigenetic contribution and the epigenetic clock in paediatric IBD

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Objectives and Study: Gene-environment interactions are strongly implicated in the pathogenesis of Inflammatory Bowel Disease (IBD). Previous work from our group has defined the circulating IBD methylome, a characteristic series of genome-wide alterations in DNA methylation in both paediatric and adult-onset IBD [1, 2]. The aims of this project are to further assess the factors shaping the epigenetic alterations in paediatric IBD, specifically the inter-generational contribution to DNA methylation alterations and the role primary, secondary or tertiary cigarette exposure may play on developmentally induced DNA methylation marks in exposed offspring. We also assess if premature biological age acceleration is observed in our paediatric IBD cohort using the epigenetic clock.

Methods: Whole blood DNA methylation profiling was performed on 90 trio families using the Illumina Infinium MethylationEPIC beadchip; assessing methylation at 850,000 sites across the genome. Each trio consisted of a paediatric IBD patient (59 CD, 28 UC, 2 IBDU) and both parents, with self-reported smoking behaviour classified as either current, former, or non-smoker. For IBD children, mean age at diagnosis and mean duration of disease (yrs) were 11.2, 1.3 for CD; 10.2, 1.7 for UC; and 12.1, 2.4 for IBDU. Methylation data was processed using minfi and limma, with batch correction using comBat and cell type deconvolution using the Houseman method. P values were corrected for multiple testing using the Benjamini-Hochberg. A secondary cohort of newly diagnosed paediatric CD patients and aged matched controls was used to calculate age acceleration using the Horvath epigenetic clock [3].

Results: We observed a strong bias towards the development of UC compared to CD in children exposed to parental smoking (2 non-exposed children with UC vs 26 exposed; 30 non-exposed CD children vs 30 exposed; OR=13, 95%CI=2.83,59.72, Fishers exact P=8.02×10^-6). We found a 4.1% methylation increase between tobacco-exposed children with CD compared to non-exposed children with CD at CpG sites within the gene encoding the repressor of aryl hydrocarbon receptor AHRR(P=0.00011), a locus typically hypomethylated by active and passive smoke exposure [4]. Stronger correlations were seen at this locus between father and child, than between mother and child. No dominant parental contribution was found at any of the known IBD methylation loci which had previously been detected in the children. Epigenetic clock analysis demonstrated biological mean age acceleration in both CD of 3.7 yrs and UC 1.6 yrs in patients compared to the non-IBD controls (P=0.0006, P=0.001). A total of 23 (25%) children demonstrated age acceleration of greater than 5 yrs of which 3 children were greater than 10 yrs.

Conclusions: These data provide new evidence for an important parental influence on disease phenotype in paediatric IBD; and new insights into the potential mechanistic role of passive smoking exposure in disease pathogenesis. Premature biological ageing may be a common consequence of early-onset IBD.

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Anti-TNF Versus Immunomodulators as First Maintenance Therapy in Paediatric Crohn’s Disease: A Multi-Centre Prospective Cohort Study With Propensity Score Matching

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Objectives and Study: TNF antagonist (aTNF) therapy is increasingly used in Canada as primary therapy to induce and/or maintain remission of Crohn’s disease (CD). This is a change in practice pattern from the traditional role of aTNF therapy reserved for cases of immunomodulator (IM) failure. This study compared outcomes with IM versus aTNF-based first maintenance therapy in paediatric luminal CD.

Methods: This was a prospective cohort study from the Canadian Children IBD Network (CIDsCaNN) of newly diagnosed children with CD aged 2-17 years. This analysis included patients with luminal inflammatory CD receiving IM or aTNF-based first maintenance therapy, following induction with steroids, exclusive enteral nutrition, or aTNF. The primary outcome was a composite of sustained steroid-free clinical remission (weighted Pediatric CD Activity Index <12.5 from 6 to 18 months after therapy start) and endoscopic remission (absence of ulcers on endoscopy, or normal magnetic resonance enterography, if isolated small bowel disease and no repeat endoscopy) at 18 months on first maintenance therapy. Logistic regression modeled the propensity of receiving aTNF maintenance therapy, and a 1:1 Greedy matching, without replacement, within a caliper width equal to 0.2 of the standard deviation of the logit of the propensity score, was used to match participants who received aTNF with those who received an IM. Missing data were imputed using multiple imputation with the fully conditional specification prior to matching. To account for clustering by centre, outcomes were analyzed with generalized estimating equations in the entire cohort and linear mixed models in the matched cohort.

Results: Among 898 children with CD enrolled in the inception cohort between 01/2014 and 12/2018, 532 met inclusion criteria and received IM (N=293) or aTNF (N=239) as first maintenance therapy. Despite greater CD activity at diagnosis among children receiving aTNF as first maintenance (Table 1), the primary endpoint was more often met with aTNF vs IM maintenance (20% vs 2%, odds ratio (OR) 14.8, p<0.001) and similarly in the matched cohort (26% vs 7%, OR 5.2, p<0.001). More children in the aTNF group achieved each of sustained steroid-free clinical remission (37% vs 8%, OR 7.2, p<0.001 in the entire cohort; 30% vs 9%, OR 4.4, p<0.001 in the matched cohort) and endoscopic remission (51% vs 9%, OR 10.4, p<0.001 in the entire cohort; 56% vs 15%, OR 7.2, p<0.001 in the matched cohort) on first maintenance therapy at 18 months. Children in the aTNF group received fewer steroid courses from 6-18 months (incidence rate ratio 0.23, 95%CI 0.1-0.5, in the entire cohort and 0.24, 95%CI 0.1-0.6, in the matched cohort). For children with Tanner stage I-III, the mean 18-month increase in height z-score was greater in the aTNF group compared to the IM group, this reached significance only in the matched cohort (0.26 vs 0.10, p=0.060, in the entire cohort; 0.30 vs 0.14, p=0.041 in the matched cohort).
Conclusions: In this study, aTNF was superior to IM as first maintenance therapy in paediatric luminal CD. The observed greater likelihood of clinical and endoscopic remission may help advocate for better access and funding for early aTNF therapy in paediatric CD. A substantial portion of patients failed to meet the primary outcome, despite early aTNF therapy, which reveals an unmet need in paediatric CD.

Conflict of Interest: Rilla E. Schneider: None; Kevan Jacobson: Advisory board: AbbVie, Janssen, Merck, Amgen, Mylan; speaker’s bureau: AbbVie Janssen; investigator-initiated research support: Janssen.
Hien Q. Huynh: Advisory board: AbbVie, Janssen, Merck, BioJamp; speaker: AbbVie, Janssen; Fresenius Kabi; investigator initiated research support: Janssen, AbbVie; research site investigator: Pfizer, Takada and AbbVie (Allergan).
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Colette Deslandres: Advisory board: AbbVie, Janssen; speaker: AbbVie, Janssen; moderator: AbbVie, Janssen, Pfizer.
Jennifer deBruyn: Advisory board: AbbVie, Amgen, Janssen, Mylan, Merck; speaker: AbbVie.
Wael El-Matary: Advisory board: AbbVie, Janssen, Merck; investigator-initiated research support: Janssen; speaker: AbbVie.
Anthony R. Otley: Advisory Board: Janssen and AbbVie; consultant: AbbVie, Pfizer; investigator-initiated research support: AbbVie; research site: AbbVie, Pfizer, Eli-Lilly.
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Mary Sherlock: Advisory board: AbbVie, Janssen; speaker: AbbVie, Janssen.
Jeffrey Critch: Consultant: AbbVie, Pharma Science.
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O-009

Tofacitinib in pediatric ulcerative colitis: a retrospective multi-center experience from the Paediatric IBD Porto group of ESPGHAN


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Objectives and Study: Tofacitinib, a Janus kinase (JAK) inhibitor, has recently been approved for the treatment of moderate to severe active ulcerative colitis (UC) in adults. Data on efficacy and safety in pediatric patients are limited. In this multicenter study from the Paediatric IBD Porto group of ESPGHAN, we describe the short-term effectiveness and safety of tofacitinib in an international pediatric IBD cohort.

Methods: Retrospective review of children (2-18 years) diagnosed with UC treated with tofacitinib from 15 pediatric centers internationally. The primary outcome was corticosteroid-free clinical remission (PUCAI<10) at week 8, with secondary outcomes including clinical response (≥20 point decrease in PUCAI), colectomy rate, and safety. The primary outcome was calculated utilizing non-response imputation (NRI), whereby drug cessation for any reason was considered a treatment failure.

Results: 78 patients (43 (55%) female, mean age at diagnosis 12.5 (±2.7) years, median disease duration 20 months (IQR 10.3-38.8)), all with previous biologic failure, including 20/78 (26%) with the previous failure of three biologic classes. 15/78 (19%) patients achieved corticosteroid-free clinical remission at week 8 with a further 18/78 (23%) demonstrating clinical response. 9/78 (12%) underwent colectomy by week 8, and 21/78 (27%) by week 24. Twelve adverse events were reported including five infectives (three of which deemed possibly related to treatment – zoster, HSV-2 cheilitis, and septic arthritis), one case of pancreatitis, and abnormal blood test results in 5 children (anemia, lymphopenia, elevated hepatic transaminases and hypercholesterolemia).

Conclusions: In this largest real-life cohort of tofacitinib in pediatric UC to date, tofacitinib seemed effective in at least 19% of highly refractory patients by week 8. Adverse reactions and safety were largely consistent with adult data.
Poster Presentations

P-001 (Poster of distinction)

Pro-inflammatory and epithelial barrier-modulating effects of specific dietary fibres are dependent on the dietary fibre source and interaction with gut microbiota

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Objectives and Study: Dietary fibers are not digested in the bowel; they are fermented by microbes, typically promoting gut health. However, IBD patients experience sensitivity to consumption of fibers. Our previous findings offered the first mechanistic evidence demonstrating that unfermented dietary β-fructans (inulin and oligofructose) can induce pro-inflammatory cytokines in a subset of paediatric IBD colonic biopsies cultured ex vivo. Incubating oligofructose with whole-microbiota intestinal washes from non-IBD or remission IBD patients improved fermentation and reduced pro-inflammatory responses, but not from patients with active disease. Fibre-induced immune responses correlated with microbe functions, luminal metabolites, and fibre avoidance. Here we aimed to expand on our findings and identify inflammatory and epithelial barrier responses to a series of dietary fibres isolated from common fruits, grains, and vegetables.

Methods: Agriculturally relevant fibres extracted from food items (e.g., fruits, vegetables, grains) were profiled to determine the relationship between fibre structural properties and host response. Colonic biopsies (IBD and non-IBD) cultured ex vivo, primary blood cells, and cell lines were incubated with fibre isolates and immune responses (cytokine secretion [ELISA/MSD] and expression [qPCR]) and epithelial barrier repair (trans epithelial electrical resistance; TEER) were assessed. Fibres were cultured in anaerobic chamber with IBD or non-IBD whole gut microbiota (mucosal brushings); fermentation supernatants were used to treat primary blood cells and cell lines to determine the effects of fermentation on immune and epithelial responses. Taxonomic classification of microbial fermentation cultures was conducted with Kraken2 and metabolic profiling by HUMAnN2, using R software. HPLC and gas chromatography volatile fatty acid (CG-VFA) analysis were used to identify concentrations of remaining fibre and SCFAs following anaerobic fermentation.

Results: β-fructan and arabinoxylan fibres produced the most significant pro-inflammatory responses (e.g., cytokine secretion), while β-fructan and pectin fibres promoted improved epithelial barrier formation, and β-glucan fibres hindered epithelial barrier formation. Fermentation of fibres was prominent following culture with only non-IBD and select remission IBD patient microbiota communities, dependent of specific microbial functions; this reduction in fibre and concomitant increase in short chain fatty acids reduced the inflammatory effects of these fibres.

Conclusions: Our findings suggest that intolerance and avoidance of specific fiber containing foods in select IBD patients is associated with the inability to ferment these fibers, mediated by altered microbial functions (enzymes), leading to worsened inflammation and alterations in gut epithelial barrier integrity. Both the type of fibre and agricultural source of the fibre determines host response and interaction with patient gut microbiota communities. Our work highlights select disease state scenarios in which administration of fermentable fibers should be avoided in IBD patients and tailored dietary interventions considered in order to increase consumption of ‘safe’ dietary fibres.
Efficacy and Safety of Ustekinumab in paediatric Inflammatory Bowel Disease: a quaternary centre experience

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Objectives and Study: Few studies have reported efficacy and safety of Ustekinumab in children with inflammatory bowel disease (IBD). The aim of our study is to assess efficacy and safety of Ustekinumab in paediatric patients with IBD including Crohn’s Disease (CD) and Ulcerative Colitis (UC) after treatment failure with previous first-line biologic agents.

Methods: All children initiated on Ustekinumab for treatment of IBD between August 2017 and April 2022 were identified. A retrospective review of records including treatment response and safety was performed. All patients received an intravenous loading dose of 6 mg/kg followed by 8-weekly subcutaneous maintenance dosage: 90 mg if weight > 40 kg or 45 mg if weight < 40 kg. Clinical activity at initiation was assessed by weighted paediatric Crohn’s Disease Activity Index (wPCDAI), Paediatric Ulcerative Colitis Activity Index (PUCAI) and 4-point ‘Improve Care Now’ Physician Global Assessment (PGA) based on severity of symptoms (1=asymptomatic; 2=mild; 3=moderate; and 4=severe). Primary outcome was clinical reduction of PGA at 8 and 52 weeks. Clinical remission was defined as a PGA of 1. Partial response was defined as PGA drop of ≥1 point. Secondary outcome was biochemical response with reduction in faecal calprotectin (FC), C reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Loss of response to Ustekinumab was defined as histologically active disease and PGA ≥3. Adverse events were recorded from initiation to end of study period.

Results: Thirty-one children were included in the study (19 Male, median age of diagnosis 7 years; range 0-16 years). CD was diagnosed in 29 and UC in 2. Ustekinumab was initiated in all 31 children due to histological confirmation of refractory disease, following anti-TNF therapy. Six children experienced additional adverse events to anti-TNF treatment prior to discontinuation. Two patients with UC, also had disease refractory to vedolizumab.

At baseline the median wPCDAI was 30 (range 10-50) and median PGA was 2 (range 2– 4).

At week 8, 52% (15/29) were in clinical remission, and 79% (23/29) had partial clinical response. Two patients did not have a documented clinical assessment at 8 weeks. There was statistical significance difference between baseline and week 8 PGA (median 2 vs 1; p<0.00001).

At week 52, 46% (13/28) were in clinical remission and 11% (3/28) showed partial clinical response. Clinical scores at week 52 were significantly lower compared to baseline (median PGA 2 vs 1, p=0.00001). Biochemical parameters at 52 weeks were available in 18 children. There was no statistical difference between baseline and 52-week FC (median 1312 vs 448, p=0.09), CRP (median 5 vs 5, p=0.07) and ESR (median 25 vs 15, p=0.07).

Three children discontinued Ustekinumab due to loss of response, after an average treatment of 18 months (range 10-30 months). No significant adverse events following initiation were reported over the study period (median 18 months, range 3-62 months).

Conclusions: Ustekinumab induces sustained clinical response in almost half of children with no significant side effects reported. Reduction in biochemical indices did not reach statistical significance, perhaps reflecting the challenge of achieving deep remission in this population.
P-003

Short-Chain Fatty Acids Affect Epithelial and Macrophage Response to the Pediatric IBD-associated Pathobiont *Bacteroides fragilis*

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Objectives and Study: Dietary fibres are fermented by the gut microbiome into various products including short-chain fatty acids (SCFA), which are important for maintaining a healthy gut. Patients with IBD have an altered microbiome, leading to changes in the gut microenvironment, including a shift in the SCFA profile. Pathobionts are commensal organisms that become pathogenic under specific conditions, likely related to microenvironmental changes within the intestinal tract. This is especially relevant to children given that early life exposures are critical to microbiome development, and the potential impact of microbes and nutrition specifically in pediatric IBD (pIBD). The objectives of our study were to: 1) determine if microbes from IBD patients are more proinflammatory compared to non-IBD microbes; and 2) define how SCFAs affect host-response to potential pathobionts.

Methods: Fructooligosaccharide (FOS) fermentation and SCFA production were assessed by HPLC-RID using whole-intestinal microbe culture collected from pIBD (n=10) and non-IBD patients (n=8). Individual anaerobic bacteria were isolated from a non-IBD and pIBD patient and screened for proinflammatory response [interleukin (IL)-1ß] using THP-1 monocytes/macrophages. Caco-2 (epithelial) or THP-1 cells were pre-exposed to individual SCFAs (50 mM acetate or formate; 10 mM succinate; or 1 mM butyrate or propionate), then infected with *B. fragilis* isolated from patients. Microscopy (bacterial staining with HEMA 3), qPCR, ELISA, TransEpithelial Electrical Resistance (TEER), and culturing were used to determine invasion potential, cytokine expression, and secretion.

Results: FOS fermentation by microbes from pIBD patients led to increased acetate and decreased butyrate production. Microbes from pIBD patients were generally more proinflammatory, with increased IL-1ß secretion and reactive oxygen species generation, compared to those from non-IBD patients. *B. fragilis* isolated from an IBD patient was found to be a potential pathobiont with increased invasion and cytokine production in both epithelial and macrophage cells. Invasion was further increased when cells were exposed to SCFAs, particularly acetate and butyrate. Furthermore, the strain isolated from the pIBD patient was observed (by microscopy) to be more adherent to the epithelial barrier, causing a loss of membrane integrity, measured by TEER. Inflammasome pathway proteins were significantly upregulated in Caco-2 cells infected with pIBD-isolated *B. fragilis* and incubated with acetate or butyrate.

Conclusions: The alerted microbiome in pIBD patients leads to a changed fibre fermentation potential with increased acetate and decreased butyrate, which likely affects host response to microbes and promotes inflammation. This changed microenvironment provides the appropriate opportunity for the development of pathobionts, such as the identified *B. fragilis* strain we isolated from a pIBD patient. The observation that acetate and butyrate increased host susceptibility to this strain indicates that understanding diet and SCFA production are instrumental in treating chronic conditions such as IBD, especially in children. The role of diet as both a treatment and potential cause of inflammation in IBD is becoming more apparent; therefore, it is crucial that we understand the complex role diet has in host-microbe interactions.
P-004

Role of miRNAs in Children with Crohn's disease in Infliximab Treatment

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Objectives and Study: Recent studies have demonstrated the critical role of microRNAs (miRNAs) alterations in the development of chronic inflammatory processes in Inflammatory Bowel Disease (IBD). Analyzing the target genes, it was identified a connection between miR-20 and miR-126 and ATP binding cassette sub-family G member 2 (ABCG2) and ATP-Binding cassette, sub-Family B 1 (ABCB1), two efflux transport proteins playing a significant role in intestinal barrier integrity, which is disrupted in IBD. The aim of our study was to evaluate the role of miR20a and miR-126 and their response to anti-TNF-α therapy in Crohn disease (CD) children.

Methods: Serum from CD patients were collected before Infliximab (IFX) therapy (T0), after induction at 8 weeks (T1) and after 6 months from IFX induction (T2). Colonic biopsies were obtained before IFX introduction (T0). IFX trough level were determined by commercially available Enzyme-linked immunosorbent (ELISA) assay. Serum and colonic miR-20a and miR-126 levels were analyzed by real-time reverse transcription PCR (qRT-PCR) and quantified by using 2^-ΔΔCt method. The activity of disease was evaluated trough the Pediatric Crohn Disease Activity Index (PCDAI) and inflammatory parameters, such as C-reactive protein (CRP), erythrocyte sedimentation rate, white blood cells count, hemoglobin and faecal calprotectin. Differences between groups were analyzed by using a Two-way Analysis of Variance (ANOVA), while the strength of association with inflammation parameters was evaluated by using Pearson correlation analysis. A p value < 0.05 was considered significant

Results: Eleven CD children treated with IFX were enrolled in the study. Serum expression of miR-20a and miR-126 resulted significantly correlated to colonic concentration at T0 (p<0.001 for both). IFX trough level at T1 and T2 negatively correlated with the serum expression of both miR-20a (r=-0.86, p<0.01) and miR-126 (r = -0.91, p < 0.01). In particular, serum miR20a and miR-126 expressions were significantly reduced at T2 (p < 0.01 for both) compared to T0. At T2 we found a significant reduction of PCR (p=0.02) and this parameter negatively correlated with IFX trough level (r = -0.80, p< 0.01), while it was positively associated with serum miR-20a (r = 0.78; p <0.05) and miR-126 (r = 0.73; p< 0.05).

Conclusions: Our preliminary results suggest that the anti-inflammatory effect of IFX therapy could be mediated by the down-regulation of serum miR-126 and miR-20-expressions.
P-005

Histologic findings at diagnosis as predictive markers of clinical outcome in pediatric Ulcerative Colitis

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Objectives and Study: Ulcerative colitis (UC) is a chronic relapsing inflammatory bowel disease. Histologic remission is one of the goals of medical therapy, as it appears to be associated with favorable clinical outcomes. However, its role at diagnosis as a possible predictive factor of disease course has not been investigated so far. Therefore, this study aimed to assess whether histologic findings at diagnosis could predict clinical relapse over time. As a secondary aim, we evaluated the correlation between clinical, biochemical, endoscopic, and histological activity scores.

Methods: This is a retrospective single-center study including pediatric UC patients diagnosed in our department with a minimum follow-up of 12 months. The correlation between the histological activity (measured with three histological indices, Nancy Index, NI; Robarts Histopathology Index, RHI; Gebboes Score, GS) and clinical outcomes [acute severe colitis episodes, reactivation of UC defined as PUCAI > 35, fecal calprotectin (FC) > 250 µg/g, need of surgery, need of systemic steroid therapy or need of step-up treatment] over a period of 12 months has been evaluated for each patient. Secondarily, we assessed the correlation between the histological and the endoscopic activity (according to the Mayo endoscopic score) and between the histological and inflammatory markers at diagnosis (erythrocyte sedimentation rate, C reactive protein, FC). Multivariate Cox regression was used to identify the correlations.

Results: Forty-nine UC patients were included. No correlation was found between clinical relapse at 1 year and the three histological indices at diagnosis (p>0.05). An excellent concordance was found between NI and GS (r: 0.909, p<0.001), moderate between GS and RHI (r: 0.737, p<0.001), and between all the histological and endoscopic indices (NI-Mayo r: 0.391; GS-Mayo r: 0.312; RHI-Mayo r: 0.328, p<0.05). Finally, no correlation was found between histologic scores and serum inflammatory markers at the diagnosis.

Conclusions: Histological findings at the diagnosis provide no information about the clinical course of pediatric UC and cannot be used as predictors of disease course. A good correlation was found among the different histological activity scores used in routine clinical practice. Further studies are needed to establish the role of histology in the clinical management of pediatric UC.
P-006

Faecal S100A12 as a non-invasive marker in Inflammatory Bowel Disease

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Objectives and Study: Calgranulin-C (f-S100A12) and zonulin are considered marker of intestinal inflammation. Our aim was to evaluate faecal S100A12(f-S100A12) and faecal zonulin (f-zonulin) as alternative markers in the follow-up of IBD children, compared with faecal calprotectin (FC) and serum inflammatory markers.

Methods: We prospectively enrolled all Crohn’s Disease (CD) and Ulcerative Colitis (UC) pediatric patients in follow up, who underwent ileocolonoscopy within the previous six months. S100A12, f-zonulin and FC were determined by enzyme-linked immunosorbent assay (ELISA).

Results: One hundred seventeen consecutive children, 39.3% with CD and 60.7% with UC were enrolled. In both CD and UC there was a direct correlation between FC and f-S100A12 levels (p<0.001 and p<0.001, respectively). In CD patients FC levels were directly correlated with CRP (p =0.046), ESR (p =0.004), fibrinogen (p=0.002), platelets count (p=0.038) and WBC count (p =0.044) and an inversely correlation with hemoglobin (p=0.044) and hematocrit (p=0.046). F-S100A12 correlated directly with CRP (p =0.046), fibrinogen (p=0.038), platelets count (p=0.021) and WBC (p=0.009) and inversely with hemoglobin (p=0.008), hematocrit (p=0.015). In UC patient FC levels correlated only with CRP (p =0.002), whereas we found a direct correlation between f-S100A12 and CRP (p=0.040) and platelet count (p=0.038). We found significant difference in FC and f-S100A12 levels between patients in clinical relapse and remission as well as for endoscopic inflammation and endoscopic remission (p=0.048 and p=0.019, respectively) in both CD and UC group.

Conclusions: Our data suggest that f-S100A12 and FC are useful non-invasive biomarkers in the management of pediatric IBD in follow up and in monitoring endoscopic and clinical relapse.
Paediatric inflammatory bowel disease patients with *Clostridioides difficile* infection have a disrupted gastrointestinal microbiome and more severe disease outcome

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Objectives and Study: Children with inflammatory bowel diseases (IBD) are particularly vulnerable to *Clostridioides difficile* infections (CDI) and experience significantly worse health outcomes including increased hospitalisation and shorter time to their first bowel resection. Previous studies have correlated these outcomes to specific gastrointestinal microbiome features. However, data regarding features that may predispose PIBD patients to CDI is lacking. Furthermore, it is not known whether CDI has long-term impacts on the microbiome of PIBD patients in remission. Consequently, our primary aims were to investigate whether PIBD-CDI patients had a distinct microbiota at baseline compared to PIBD controls and to examine whether PIBD-CDI patients had a distinct microbiome during remission than those without CDI. Finally, our secondary aim was to assess whether PIBD patients with CDI required more biologic therapy.

Methods: Patients aged 2-17 years and newly diagnosed with IBD between November 2014 and March 2019 were invited to participate. Each patient was requested to submit 4 stool samples in an interval of six months between samples and follow up continued until June 2021. Patients were divided into those that developed CDI (IBD-CDI) and those who did not (IBD controls). DNA was extracted from stool samples and the microbiota of each was profiled using 16S rRNA amplicon sequencing on an Illumina MiSeq. Data analysis was further divided into 2 cohorts: Cohort 1 represented microbiome data from samples of patients who developed CDI and were collected prior to the infection. Cohort 2 represented microbiome data from samples of patients in remission who had CDI. Alpha and beta diversity was compared to non-CDI controls within each cohort. Clinical and epidemiological data was collected at baseline and at the time of follow up. Data collected during stool collection included current medications and Pediatric Crohn Disease Activity Index (PCDAI) or Pediatric Ulcerative Colitis Activity Index (PUCAI). Hazard ratio (HR) was calculated to progression to biologic treatment and surgeries in patients who had a CDI compares to those who did not. Rate ratio (RR) of the number of hospitalisations was calculated between the groups.

Results: There were 128 PIBD patients enrolled in the study. Twenty- eight (21.9%) developed CDI. Twenty- three stool samples were sequenced and analysed and divided into cohort 1 (n=11) and cohort 2 (n=12). PIBD-CDI patients were found to have lower species richness both prior to infection and during remission. Though overall diversity was reduced in PIBD-CDI patient samples prior to infection, this was not found during remission. Patients who had CDI were more likely to progress to a biologic therapy (HR 1.85 P =0.06) and had significantly more hospitalisations (RR 2.20, P< 0.001) and surgery (HR 3.15, P= 0.019).

Conclusions: Paediatric IBD patients who developed CDI had a disrupted compositional baseline microbiota compared to those who never developed CDI. Moreover, patients who had CDI during the course of their disease developed more severe outcome with more hospitalisations and surgery.

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P-008

Gut microbiome abundance, diversity, and metabolic changes are correlated with sleep efficiency and disease phenotype in paediatric inflammatory bowel disease


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Objectives and Study: Sleep disturbances are common in patients with inflammatory bowel disease (IBD). Sleep disturbance may act as an environmental trigger for IBD disease activity. While this relationship remains poorly understood, sleep disturbances have previously been associated with increased inflammatory cytokines. Altered microbiota is a hallmark of IBD and these changes have been correlated with both altered inflammation and sleep efficiency. Here we hypothesized that disruption of the gut microbiota community in pediatric IBD patients may impair sleep efficiency, and in turn, worsen patient outcomes.

Methods: Children <17 years with an established diagnosis of IBD were assessed for sleep disturbances using a sleep diary. Patients were asked to complete a sleep diary in the week preceding their clinic appointment. The sleep diary would provide information about latency to fall asleep, number and duration of awakenings, total sleep time, and sleep quality. Participants’ clinical disease activity was assessed using pediatric Crohn disease (CD)/ulcerative colitis (UC) activity indices. Patient stool samples were collected for calprotectin measurement, and to examine microbiota (metagenomics; Kraken2-R), Short Chain Fatty Acid (SCFA; gas chromatography – volatile fatty acid analysis), and metabolic pathways (metagenomics; Maaslin2) profiles. Correlations were performed against patient fecal calprotectin (FCal), PCDAI/PUCAI, sleep efficiency, length of sleep, and time in bed. The study protocol was registered at ClinicalTrials.gov ID: NCT02970149.

Results: A total of 80 children (mean age 13.2y, 47 boys) with IBD (52 CD) were recruited. Fecal samples were available for 28 children (mean age 13.8y, 18 boys, 18 CD). Of these, 10 (36%) patients had clinically active disease with PCDAI/PUCAI > 10, and 12 (43%) patients had FCal >100ug/g. Diagnosis of CD vs UC differed in levels of microbiota and metabolites (e.g., Clostridium, Akkermansia, Blautia, serine-type carboxypeptidase and β-fructofuranosidase). Different disease phenotype was associated with different microbiota (e.g., Veillonella, Akkermansia, Allistipes) and metabolites (e.g., H-transport, NADH-dehydrogenase, 6-phosphofructokinase). Average length of sleep was associated with significant changes in microbiota diversity (e.g., Bacteroides, Enterococcus, Bifidobacterium, Allistipes, Streptococcus, Ruminococcus) and vast metabolic changes, primarily related to energy production. Finally, the SCFA propionate negatively moderately correlated with sleep efficiency (total sleep time/total time in bed; P<0.05) and total time in bed (P<0.05).

Conclusions: Our findings suggest that gut microbiota diversity, abundance, and functions (metabolites) may play an active role in disruption of sleep patterns in paediatric IBD, or alternatively that sleep disruption impacts on the gut microbiome, resulting in worsened disease phenotypes. These data support the need to further investigate causal relationships between gut microbiota, sleep efficiency, and disease outcomes in children with IBD.
P-009 (Poster of distinction)

Gut metabolomic and compositional signatures predict response to treatment with exclusive enteral nutrition in children with active Crohn’s disease

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Objectives and Study: Predicting response to treatment with exclusive enteral nutrition (EEN) in paediatric Crohn’s disease (CD) can lead to more personalised, cost-effective, and efficacious therapy. We explored the ability of pre-treatment clinical and multi-omics parameters to predict faecal calprotectin (FCal) levels at EEN completion.

Methods: In 37 children [median (IQR), 12.4y (10.1, 15.0)] with active CD, disease parameters, dietary intake, 19 inflammatory cytokines, and 92 plasma inflammation-related proteomic markers in plasma, diet-related bacterial metabolites and ¹H NMR metabolomics in faeces, as well as the faecal, duodenal, ileal, ascending and descending colon microbiome (16S rRNA sequencing), and dietary intake were measured prior to EEN initiation. Fifteen children responded to EEN (RS) and 12 not (non-RS) using a FCal cut-off <300.

Results: Disease and host immunological parameters did not predict FCal levels at EEN completion. Responders had lower fibre intake, half the concentration of butyrate, acetate, phenylacetate and higher bacterial richness, in faeces, than non-RS. A model trained with 37 discriminant duodenal operational taxonomic units (OTUs) demonstrated a sensitivity of 83% and specificity of 90% to predict RS from non-RS. The predictive ability of the faecal and the microbiomes of other mucosal sites was inferior to that of the duodenum. In multicomponent prediction including all datasets and faecal microbiome, higher levels of phenylacetate and abundance of OTU of Bacteroides, and a lower bacterial richness were predictive of non-RS with a sensitivity of 73% and specificity of 88%. Replacing the faecal with the duodenal microbiome in a subset of participants (n=14), produced a model with 100% accuracy to predict RS from non-RS. The single most important variable in this model was a Lachnospira OTU which was absent in all RS but highly abundant in non-RS.

Conclusions: We identified pre-treatment microbial signals and diet-related metabolites which may comprise targets for pre-treatment optimisation and personalised nutritional therapy in CD.

Conflict of Interest: RKR: reports speaker’s fees, travel support, advisory boards: Nestle, AbbVie, Celltrion & Pharmacosmos. RH is supported by an NHS Research Scotland Career Researcher Fellowship and has received speaker’s fees, travel support, and consultancy fees from 4D pharma. KG: reports personal fees from Nutricia, research grants and personal fees from Nestle Health Science, and personal fees from Dr Falk Pharma, Abbott, Servier, Mylan, and Baxter. The rest of the authors have no conflicts of interest to declare.
P-010 (Poster of distinction)

The bacterial and fungal microbiome of newly-diagnosed, treatment naïve children with Crohn’s disease; the modifying effects of exclusive enteral nutrition and re-introduction of habitual diet

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Objectives and Study: The fungal community (mycobiome) and immunological responses to specific fungi have been implicated in Crohn’s disease (CD) pathogenesis and its phenotype. There is limited data on profiling the mycobiome in paediatric CD and how it changes during treatment.

Methods: Fungal (ITS2) and bacterial (16S rRNA) microbiome analysis in faecal samples (n=124) from n=34 CD children before, during (30 and 60 days) and after exclusive enteral nutrition (EEN) at food reintroduction (within 60 days of EEN completion), and from 31 healthy controls were profiled. IgA and IgG anti-*Saccharomyces cerevisiae* antibodies (ASCA) analysis by enzyme-linked immunosorbent assay, in blood, was also carried out for CD patients prior to EEN initiation.

Results: The global mycobiome composition (β diversity) was different between CD and healthy children (R²=0.050; p=0.007) and presented lower Chao1 richness (mean 24.3 vs 33.0; p=0.005) for the CD cases; 13 fungal operational taxonomic units (OTUs) differed between the two groups. Similar signals were observed for the bacterial microbiome but the difference in global community structure (β diversity) was more profound than the fungal community (R²=0.094; p<0.001). Treatment with EEN induced drastic changes in mycobiome composition (β diversity), which were more profound and more variable than the effects observed for the bacterial community. Of the OTUs with abundance significantly lower in CD than healthy controls prior to EEN, one, belonging to *S. cerevisiae*, significantly decreased during EEN (compared with baseline; p<0.001 and p=0.086 at 30 and 60 days on EEN). Patients whose faecal calprotectin was low (<250 mg/kg) during food reintroduction had a lower mycobiome richness than those whose FC was raised (>250 mg/kg). 29 fungal OTUs were significantly different between these two groups in samples taken during food reintroduction, following EEN. Patients who were ASCA positive had a higher abundance of three OTUs of *S. cerevisiae*. In co-occurrence network analysis, *Simplicillium chinense*, presented significant more interactions with members of the bacterial community, particularly OTUs which changed during EEN. After participants had returned to their regular diets these microbial effects reversed and community structure moved towards that observed prior to EEN.

Conclusions: The mycobiome of children with CD present features of dysbiosis similar to the bacterial microbiome and improvement in disease condition during EEN is strongly associated with changes in its composition.

Conflict of Interest: The study was funded by Nestle Health Science
Specific microbiota drives mucosal responses in inflammatory bowel disease


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Objectives and Study: Inflammatory bowel disease (IBD) is a chronic and currently incurable condition, which is largely comprised of two main phenotypic subtypes, Crohn’s Disease and Ulcerative colitis. Abnormal immune responses to the resident gut microbiome can drive or exacerbate IBD, however, these relationships are yet to be fully elucidated. Until recently, microbiome-based studies in IBD have predominantly been restricted to high-throughput, culture-independent sequencing based analyses, typically of faecal samples. This reliance on both faecal samples and sequencing alone has limiting our understanding of host-microbiome interactions at the intestinal site of disease. Here we define key IBD-associated functional bacterial clades from within the patient microbiome, by combining shotgun metagenomic sequencing, bacterial culturing and host transcriptomic analysis with detailed experimental validation.

Methods: To achieve this, we established a paediatric IBD (PIBD) specific bacterial culture collection, comprising 6,416 isolates (207 distinct species, 79 putative novel), cultured from 286 mucosal biopsies (58 PIBD and 42 control patients). This resource, coupled with novel, high-resolution, culture-based shotgun metagenomic sequencing (231 samples) and matched host transcriptomics (231 samples) across three biopsy sites (terminal ileum, caecum, rectum) identified key, functionally distinct Enterococcus subclades associated with IBD.

Results: In vitro validation of these clades demonstrates specific differences in cell cytotoxicity and inflammatory signalling in intestinal epithelial cells, that matches the colonic mucosal response measured within the clinical patient cohort. The combination of site-specific bacterial culturing, metagenomics and host transcriptomics from patient biopsies allows identification, classification and functional validation of key microbiome species, which may be harnessed in order to aid the development of therapeutics for IBD.

Conclusions: In conclusion, this work highlights the benefits of functional clade-based bacterial analysis for the future of microbiome-based therapeutics, in the context of IBD. The Enterococcus clades identified may function as disease biomarkers or act as therapeutic candidates for a subset of IBD patients. Additionally, while these methods have allowed advancements to be made in the field of IBD, they may be employed elsewhere, with their potential use unrestricted to the gastrointestinal microbiome.

Conflict of Interest: All authors have filed patents related to this work. Samuel C. Forster has advised Microbiotica and Biomebank Australia in the development of live biotherapeutics.
Fecal microbiota in orofacial granulomatosis

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Objectives and Study: Orofacial granulomatosis (OFG) is a rare chronic inflammatory condition, characterised by granulomatous inflammation in the orofacial area. Symptoms include lip swelling and oral ulcerations. The oral manifestations of OFG cannot be distinguished from the ones of oral Crohn’s disease (CD). It is under debate, whether OFG is a condition of its own or merely a subtype of CD. Fucosyltransferase 2 (FUT2) is a gene, which is involved in the creation of H antigen, precursor of ABO-blood group antigens. These antigens are also present in the intestine, and non-secretor genotype has previously been associated with an increased risk for CD.

Previously, OFG and CD with oral manifestations were associated with an increase in Streptococcus Salivarius in salivary microbiota. However, no studies regarding the relation of faecal microbiota and OFG have been made so far. Therefore, we conducted a study to examine, whether the faecal microbiota differs between OFG patients, patients with CD and healthy controls. We also examined whether FUT2 non-secretor status is associated with OFG.

Methods: We traced 42 patients with OFG and 29 participated (median age 14.4 years, median time since diagnosis 3.0 years), as well as 24 patients with CD (median age 22.0 years, median time since diagnosis 8.95), and 20 healthy controls (median age 21.8 years) undergoing oral and dental examination. All participants provided a faecal sample and a salivary sample for DNA analysis. We investigated the FUT2 genotype in all participants. The intestinal microbiota was analysed using Illumina Miseq.

Results: We had 23 patients with OFG with CD and 6 patients with OFG but no signs of intestinal disease. The patients with OFG were grouped together for statistical power. We found that the faecal microbiota in OFG group differed substantially from healthy controls and CD patients. Clostridia were decreased in patients with OFG, when compared to patients with CD and healthy controls. Also, family Ruminococcaceae and genus Roseburia were decreased in OFG when compared to CD or healthy controls, whereas the genus Blautia was increased in OFG patients. When compared to healthy controls, patients with OFG had lower relative abundance of Faecalibacterium and Kineothrix. We found no association with FUT2 secretor- or non-secretor genotype with OFG.

Conclusions: The microbiota significantly differed not only between patients with OFG but also between patients with OFG and CD. This further supports the theory that OFG is, in fact, a condition of its own rather than a subtype of CD.
P-014 (Poster of distinction)

Tryptophan metabolite changes with diet-induced remission in paediatric crohn’s disease

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Objectives and Study: Crohn’s Disease Exclusion Diet combined with Partial enteral nutrition (CDED+PEN) and exclusive enteral nutrition (EEN) reduce dietary exposure to foods that might negatively impact the microbiome and the intestinal innate immunity. These diets induce remission in pediatric Crohn’s disease (CD) patients, but CDED+PEN is better tolerated and able to sustain remission. Although the specific mechanisms of nutritional therapy are still unknown, microbiome community changes are strongly associated with the therapeutic outcome. Metagenome studies have associated CD with amino acid metabolism. Tryptophan (Trp) is an essential amino acid, which is obtained from protein-rich diets. Trp is necessary for protein synthesis and the formation of serotonin and melatonin. Alterations in the serotonin-melatonin pathway were observed in colitis. More than 90% of dietary Trp is metabolized through the kynurenine pathway. kynurenine pathway metabolites such as kynurenine and quinolinic acid have been suggested to play a role in modulating the intestinal immune response.

Methods: We investigated changes in 20 Trp metabolites in fecal samples from a 12-week prospective trial comparing CDED+PEN vs EEN for induction of remission in mild to moderate pediatric CD. After 6 weeks, the EEN group could return to a free diet with 25% of calories from PEN. Endpoints of the study were intention to treat (ITT) remission at week (W)6 (defined by Pediatric Crohn’s Disease Activity Index (PCDAI) < 10) and corticosteroid-free ITT sustained remission at W12. A targeted measurement of Trp metabolites at W0, W6 and W12 of 75 samples was performed by liquid chromatography coupled with mass spectrometry and analyzed according to clinical outcome groups of baseline (W0), induced remission (W6_rem), no-remission (W6_nr), sustained remission (W12_sr) and non-sustained remission (W12_nsr).

Results: There were no differences in PCDAI score or tryptophan metabolites between CDED+PEN and EEN at baseline (n=15 and 13, respectively). CDED+PEN induced remission in 13 out of 15 patients (87%) at W6 (n= 15 or 9 at W6 or W12, respectively), which was maintained in 8 out of 9 patients (88%) at W12. In the EEN group, 9 out of 13 patients (69%) achieved remission at W6 (n=13 or 9 at W6 or W12, respectively) and 6 out of 9 patients (66%) maintained remission until W12. In CDED+PEN, the drops in some components of the kynurenine pathway such as kynurenine (P=9.67E-4) and quinolinic acid (P= 0.04) were strongly associated with W6_rem, which were maintained in W12_sr (P= 0.003 and 0.02, respectively). In EEN, a significant decrease in quinolinic acid levels was also associated with W6_rem (P= 0.02) and W12_sr (P= 0.03) remission, but not with W6_nr and W12_nsr. Remarkably, serotonin pathway metabolites such as melatonin, N-acetylsertotonin and 5-OH-tryptophan, were significantly increased in patients maintaining remission at W12 with both CDED+PEN and EEN. However, in patients failing to sustain remission, no significant changes were observed. There were no changes in other Trp metabolites.

Conclusions: This study suggests the reduction in kynurenine pathway compounds and the increase in serotonin pathway compounds as one of the factors mediating diet-induced and sustained remission. Further studies are warranted to explore the effect of these changes in the dietary treatment of CD.
P-015

Genetic and epigenetic analyses of the Japanese very early onset IBD

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Objectives and Study: IBD is caused by an interaction of various factors, such as genetic backgrounds, environmental factors, changes in the immune system, and intestinal microbiota. In particular, very early onset IBD (VEO-IBD), diagnosed at less than 6 years of age, is strongly influenced by genetic factors. Monogenic IBD is a type of enteritis caused by a single pathogenic variant and various causative genes have already been identified, though entire vision is yet to be elucidated. This study aims to identify such genetic factors for Japanese VEO-IBD. We also explored epigenetic alterations in the inflamed lesions.

Methods: This study was approved by our institutional review board. Peripheral blood samples were obtained from the patients with suspected monogenic IBD and their first-degree relatives, after obtaining their informed consents. Initially, we analyzed the IBD patients using a panel-sequencing of IBD-related 20 genes at a clinical laboratory, Kazusa DNA Research Institute (Chiba, Japan). For those patients who have not been diagnosed by the panel sequencing, we then conducted whole-exome and/or whole-genome sequencing to detect novel candidate genes causative for the IBD. In addition, we performed epigenetic alterations in the inflamed lesions of the patients.

Results: From 2018 to 2021, we have conducted whole-exome and/or whole-genome sequencing of 36 families with VEO-IBD patients covering 104 samples with suspected monogenic IBD. In the trio analysis, we identify several candidate genes, such as BCL6, ATF6B, BIRC6, SIK3, and HOXD3. We also found sister IBD cases who possess a heterozygous splicing variant, SLCO2A1:c.940+1G>A. Homozygous pathogenic variants of the SLCO2A1 are known to be causative for the chronic enteropathy associated with SLCO2A1 (CEAS), though it has not been known whether the heterozygous variant plays a role in the pathogenesis of other IBD. We examined mRNA and protein expression levels of the SLCO2A1 in the endoscopically resected specimens. We observed attenuated expression of the SLCO2A1 in the inflamed lesions of these patients as compared with controls. When conducting bisulfite-sequencing of the SLCO2A1, we found dense methylation of the promoter region of the SLCO2A1 only in the inflamed lesions of these cases. Since SLCO2A1 encodes a prostaglandin transporter, we next analyzed major metabolites of the prostaglandin E and M (t-PGEM) in their urine. We found much higher levels of the metabolites for the younger sister case who showed much severe symptom than the elder one; the t-PGEM levels of the younger sister case was comparable to the ones of CEAS cases.

Conclusions: These results prompted us to understand important roles of genetic as well as epigenetic alterations in the development of IBD.
P-016

Faecal pH and short-chain fatty acids are objective and discriminatory biomarkers of compliance to exclusive enteral nutrition.


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Objectives and Study: Exclusive enteral nutrition (EEN) is often used in nutritional rehabilitation and as induction therapy in active Crohn’s disease. Despite its widespread clinical use, there are currently no reliable biomarkers to objectively assess compliance. This study explored the use of faecal parameters as putative biomarkers of EEN compliance in healthy volunteers.

Methods: Healthy adults were recruited from the community. Participants were asked to replace all or part of their daily energy requirements with polymeric formula (Modulen IBD, Nestle©) for 7 days, forming four groups: a) 100% EN, b) 85% EN, c) 50% EN, or d) 20% EN. Faecal samples were collected before and after the intervention. Dietary intake was recorded with estimated weight food diaries. pH, Bristol stool chart score, water content, short chain fatty acids (SCFAs): acetate (C2), propionate (C3), butyrate (C4); and branched chain fatty acids (BCFAs): isobutyrate (IC4), isovalerate (IC5) were measured in faeces. Receiver operating characteristic (ROC) curve analysis with subset cross-validation and machine learning classification were used to define optimal cut-off values for group assignments using faecal parameters at the end of dietary intervention. For ROC curve analysis, sensitivity, specificity, and positive predictive values (PPVs) were primarily used to identify optimal cut-off values.

Results: 61 (31 females, 30 males) adults (mean age (SD): 25.9 (4.3) years) were recruited (25 to 100% EN, and 12 to each of 85% EN, 50% EN, and 20% EN groups). Estimated EN intake was 96%, 86%, 50% and 20% of average energy intakes in each group, respectively. A higher proportion of EN intake was associated with a greater increase of faecal pH and concentration of BCFAs at the end of the intervention, and with a lower concentration of SCFAs. Among all faecal parameters measured, faecal pH and the ratio of BCFAs to either C2 or C4 performed the best to differentiate between the groups (Table 1). Faecal pH>8 after the intervention had an AUC of 0.91 (p<0.001) with a sensitivity, specificity and PPV of 84%, 86% and 81%, respectively to differentiate between 100% EN vs all other groups. Likewise, a ratio of BCFAs to C4> 0.63 produced a sensitivity, specificity and PPV of 100%, 75% and 75%, respectively to differentiate between 100% EN vs all other groups (Table 1). Machine learning algorithms identified the same predictors with similar cut-off values for group assignment.
### Table 1: Receiver operating characteristic (ROC) curve analysis results for best prediction of group assignments from single 7-day faecal measurements

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Optimal cut-off</th>
<th>Positive class</th>
<th>Negative class</th>
<th>AUC</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV, %</th>
<th>NPV, %</th>
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</thead>
<tbody>
<tr>
<td>IC5/C4</td>
<td>0.362</td>
<td>100% EN (n=25)</td>
<td>non-100% EN (85% EN+50% EN+20% EN; n=36)</td>
<td>0.90</td>
<td>100</td>
<td>75</td>
<td>74</td>
<td>100</td>
<td>&lt;0.001</td>
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<tr>
<td>BCFAs/C4</td>
<td>0.630</td>
<td>100% EN (n=25)</td>
<td>non-100% EN (85% EN+50% EN+20% EN; n=36)</td>
<td>0.90</td>
<td>100</td>
<td>75</td>
<td>74</td>
<td>100</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pH</td>
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<td>100% EN (n=25)</td>
<td>non-100% EN (85% EN+50% EN+20% EN; n=36)</td>
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<td>86</td>
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<tr>
<td>IC4/C2</td>
<td>0.039</td>
<td>100% EN (n=25)</td>
<td>85% EN (n=12)</td>
<td>0.89</td>
<td>92</td>
<td>83</td>
<td>92</td>
<td>83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pH</td>
<td>8.1</td>
<td>100% EN (n=25)</td>
<td>85% EN (n=12)</td>
<td>0.78</td>
<td>76</td>
<td>75</td>
<td>86</td>
<td>60</td>
<td>0.001</td>
</tr>
<tr>
<td>%SCFAs</td>
<td>2.093</td>
<td>85% EN (n=12)</td>
<td>non-85% EN (50% EN+20% EN; n=24)</td>
<td>0.83</td>
<td>75</td>
<td>96</td>
<td>90</td>
<td>88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pH</td>
<td>7.8</td>
<td>85% EN (n=12)</td>
<td>non-85% EN (50% EN+20% EN; n=24)</td>
<td>0.87</td>
<td>67</td>
<td>96</td>
<td>89</td>
<td>85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pH</td>
<td>7.6</td>
<td>85% EN (n=12)</td>
<td>non-85% EN (50% EN+20% EN; n=24)</td>
<td>0.87</td>
<td>75</td>
<td>88</td>
<td>75</td>
<td>88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pH</td>
<td>7.3</td>
<td>50% EN (n=12)</td>
<td>20% EN (n=12)</td>
<td>0.82</td>
<td>75</td>
<td>92</td>
<td>90</td>
<td>79</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Abbreviations used:** AUC – Area Under the Curve; BCFAs – Branched Chain Fatty Acids; C4 – Butyrate; IC5 – Isovalerate; NPV – Negative Predictive Value; PPV – Positive Predictive Value; SCFAs – Short-Chain Fatty Acids

**Conclusions:** During treatment with EEN, faecal measurements of pH and the expression of BCFAs to C2 or C4 may be used as objective compliance markers in clinical medicine and in research. Replication of these findings in larger studies and with inclusion of participants with conditions for which EN is prescribed as a treatment, such as Crohn’s disease, is required next.
Partial enteral nutrition use for Crohn’s disease management: a systematic review

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Objectives and Study: Exclusive enteral nutrition (EEN) is an established treatment for the induction of clinical remission in children with active Crohn’s disease (CD). However, the benefit of partial enteral nutrition (PEN), in which only a part of diet is replaced with enteral nutrition formula, is not well-documented for the management of CD. This systematic review explored the effectiveness of PEN as a sole or adjuvant induction and maintenance therapy in patients with CD.

Methods: The protocol for this review was registered on PROSPERO (https://www.crd.york.ac.uk/prospero/, protocol ID: CRD42021239325). Literature search was conducted using PubMed, Ovid Embase, Cochrane Controlled Register of Trials and Cumulative Index to Nursing and Allied Health Literature electronic bibliographic databases. Two researchers evaluated each paper separately and when needed, consensus was resolved by a third.

Results: 56 articles met the inclusion criteria, grouped under the following six distinct areas for PEN use for CD management: 1) as induction treatment; 2) as maintenance treatment; 3) for prevention of post-operative recurrence; 4) for prevention of loss of response (LOR) to anti-TNFα therapies; 5) for nutritional rehabilitation; and 6) for improving the quality of life. There is some low-quality evidence to suggest that PEN may improve disease activity in patients with active CD; albeit a higher proportion of energy intake from enteral nutrition formula is associated with better effectiveness. Early good quality evidence suggests that PEN combined with exclusion diets might be effective for treatment of active CD. However, most of the available studies originate from the same research group, and the additional benefits of exclusion diets, over PEN, are still unclear particularly with most studies using either high PEN volumes (up to 75% of energy requirements), or EEN prior to PEN initiation. Good quality evidence shows that PEN, at high volume (e.g., ≥35-50%) may prolong medically or surgically induced remission and improve nutritional status of patients with malnutrition or growth delay. Low-quality evidence suggests that PEN may improve response and remission rates to infliximab therapy and infliximab escalation therapy in CD. Three retrospective studies found that concomitant PEN use with anti-TNFα therapies could prevent LOR. Some evidence suggests that PEN is associated with better quality of life of patients with active disease or in remission.

Conclusions: PEN may have various clinical applications to the various aspects of CD management; however, there is need for more RCT before specific recommendations can be made.
Circulating levels of WISP-1 (Wnt1-Inducible Signaling Pathway Protein 1) and other selected adipokines in children with inflammatory bowel disease

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Objectives and Study: Wnt1 inducible protein-1 signaling pathway (WISP-1) is a relatively new adipokine involved in many cellular processes, including epithelial mucosa healing. The aim of the study was to compare circulating levels of WISP-1 and other selected adipokines [adiponectin, resistin and retinol-binding protein 4 (RBP-4)] in children with inflammatory bowel disease (IBD) with healthy controls and to investigate possible differences between Crohn’s disease patients (CD) or ulcerative colitis (UC).

Methods: The study was performed as a case-control study. In addition to adipokines, anthropometric, lipid parameters, markers of inflammation or disease activity were evaluated in all participants.

Results: Compared to healthy controls (n=20), significantly lower levels of adiponectin and higher levels of resistin and WISP-1 were found in patients with IBD (n=58) - figure 1. Elevation of WISP-1 was detected only in the CD group (2917 (740-5198) pg/ml) compared to UC group (373 (49-3004) pg/ml) and healthy controls (311 (38-1905) pg/ml). There were no differences in RBP-4 levels between the groups. Adiponectin, WISP-1 and RBP-4 were independently associated with body mass index only, resistin levels were associated with C-reactive protein levels and leukocyte counts.

Conclusions: Adverse adipokines production reflects presence of dysfunctional fat tissue in IBD patients. Higher levels of WISP-1 in CD compared to patients with UC may indicate a specific role for mesenteric adipose tissue in WISP-1 production.

This research was supported by MH CZ DRO (FNOI, 00098892).
P-019

Impact of exclusive enteral nutrition vs. steroid induction therapy on transmural healing in pediatric patients with Crohn Disease

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Objectives and Study: To compare the impact of exclusive enteral nutrition (EEN) and steroid on transmural healing in pediatric Crohn disease patient.

Methods: We conducted a retrospective monocentric observational study at the Paediatric Gastroenterology Unit of Umberto I Hospital in Rome. We enrolled pediatric CD patients (age at diagnosis < 18 years) in maintenance therapy with azathioprine (AZA) between January 2010 and April 2021 with a minimum follow-up of 12 months. We divided patients into two cohorts based on the induction therapy: one (n = 45) received methylprednisolone (CS group), and the other group (n = 35) EEN (EEN group). Transmural healing was defined as wall thickening < 3 mm, absence of ulcers, fistula, and perianal disease at MRE.

Primary outcome of the study was to compare the impact of EEN and CS in inducing TH at 6 and 12 months. Secondary outcomes were to compare, in children treated with CS or EEN as induction therapy, rates of MH, relapses, complications (stenosis, fistula), surgery, clinical (wPCDAI), and biochemical response.

Results: 80 patients were enrolled. At 6 months TH was achieved in 13 patients with EEN (37.7%) and 8 patients with CS (17.7%) (p=0.005). At 12 months 10 patients with EEN (28.6%) and 7 patients with CS (15.5%) reached TH (p=0.17). No significant difference was found for MH rates at 6 months in the two cohorts [9 (25.7%) patients with EEN vs. 12 with CS (26.6%), p=1], while at 12-month follow-up 14 children treated with EEN (40%) were in MH, compared to 6 (6.6%) initially treated with CS (p=0.003). No statistically significant differences were observed for disease relapses, hospitalizations, complications, surgery, step-up therapy, auxologic parameters, biochemical and clinical response.

Conclusions: In pediatric CD patients in maintenance with AZA, induction therapy with EEN is related with higher rates of TH than CS in the short-term. This difference disappears after 1 year of follow-up. Larger and prospective studies are necessary to evaluate the long-term effects of induction therapy on the natural history of CD.
Utility of the Endoscopic Healing Index in a cohort of pediatric Crohn’s Disease

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Objectives and Study: Noninvasive tests to assess endoscopic healing (EH) in Crohn’s disease (CD) are an important adjunct to achieving this target. The Endoscopic Healing Index (EHI, Prometheus Laboratories Inc.) was developed in adults to identify EH based on serum levels of 13 proteins. This index has not been assessed in children and we thus aimed in this prospective study to explore the utility of EHI in pediatric CD.

Methods: Serum samples from children undergoing ileocolonoscopy as part of two prospective cohorts, the ImageKids study and the BioBank at Shaare Zedek Medical Center, were submitted for proteomics analysis using the EHI at Prometheus laboratories. Stool was collected for fecal calprotectin (FC). As determined in adults, we defined EH as EHI<20, active disease as EHI ≥50, while EHI 21-49 represents a gray zone, and EH is consistent with active disease. The index was compared with SES-CD-defined EH (i.e., <3 points) and other constructs of disease activity including the Mucosal Inflammation non-Invasive MINI index, CRP (mg/L), fecal calprotectin, and wPCDAI.

Results: One hundred seventy-four pediatric CD patients were included (93, 53%) males, median age at diagnosis 12.5 years (IQR 10.3-14.1), median disease duration 1.7 years (IQR 0.3-3.4) and 38/171 (22%) with SESCD<3. Twenty six children (15%) had an EHI<20, 73 (42%) had an EHI 21-49 and 75 (43%) an EHI ≥50. The EHI identified patients with SESCD<3 with an area under receiver operating characteristic curve (AUROC) of 0.71 (95%CI 0.62-0.81, Figure 1). EHI<20 had sensitivity 90% and specificity 26% for detecting EH and EHI>50 identified active disease with sensitivity 48% and specificity 79%. In our cohort the optimal cutoff for sensitivity and specificity was achieved at 32 points (sensitivity 75%, specificity 63%).

The EHI had fair correlation with SESCD (r=0.36, p=<0.001) and wPCDAI (r=0.33, p=<0.001); moderate correlation with CRP (r=0.56, p=<0.001) and calprotectin (r=0.56, p=<0.001); and good correlation with the MINI index (r=0.64, p=<0.001, n=125 patients). The AUROC values for the other constructs to reflect EH were 0.89 (0.82-0.96) for the MINI index, 0.73 (95%CI, 0.63-0.82,) for CRP, 0.90 (95%CI, 0.84-0.96) for calprotectin (n=129), and 0.71 (0.63-0.80) for the wPCDAI (Figure 1).
Conclusions: Sensitivity of the EHI in this pediatric cohort was similar to that found in adult CD patients, however specificity was slightly lower. Overall, EHI performed similarly to wPCDAI and CRP and worse than the MINI index and calprotectin. Correlation between EHI and the MINI index was very good. A cutoff of 32 points should be further explored in the pediatric population.

Conflict of Interest: AMG: received during the past 3 years consultant fees from Abbvie, Amgen, Bristol Myers Squibb, Lilly, Janssen, Merck, Pfizer; speaker fees from Abbvie, Janssen, Nestle; investigator-initiated research grant from Abbvie
DT: received last 3 years consultation fee, research grant, royalties, or honorarium from Janssen, Pfizer, Hospital for Sick Children, Ferring, Abbvie, Takeda, Atlantic Health, Shire, Celgene, Lilly, Roche, ThermoFisher, BMS
GF: received last 3 years consultation fee from Abbvie and Lily
EOM: received last 3 years speaker fees from Takeda and Abbott
P-021

Hydrogen sulfide metabolizing enzymes in the intestinal mucosa in pediatric and adult inflammatory bowel disease

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Objectives and Study: Hydrogen sulfide (H2S) is a long-known toxic gas that has recently been attributed many important regulatory functions. In the colon, H2S can be produced and detoxified endogenously. Both too little and too much H2S exposure is associated with inflammatory bowel disease (IBD), a chronic intestinal disease divided into Crohn's disease (CD) and ulcerative colitis (UC). As the pathogenesis of IBD still remains elusive, the aim of this study was to investigate possible differences in the expression of these enzymes in aging and IBD.

Methods: 149 intestinal mucosal biopsies from terminal ileum, ascending colon and rectum of 25 adults and 22 children with CD or UC, as well as 26 healthy controls, were stained immunohistochemically for cystathionine-g-lyase (CSE), 3-mercapto-sulfurtransferase (3-MST), ethylmalonic encephalopathy 1 protein (ETHE1), Sulfide:quinone oxidoreductase (SQOR) and thiosulfate sulfurtransferase (TST). The expression level was determined by multiplication of staining intensity and percentage of positively stained cells.

Results: Healthy adults showed lower expression of all H2S synthesizing and detoxifying enzymes than healthy children. Adults with IBD had a significantly lower expression of ETHE1, CSE and 3-MST compared to healthy controls; the UC group also had a lower expression of TST. There was less difference in the expression between children with IBD compared to controls, but still a lower expression was seen.

Conclusions: These results indicate an age-related decrease in the expression of H2S synthesizing and detoxifying enzymes. Adults with IBD, however, showed a dysfunctional H2S metabolism. Whether this is causative of or resulting from the disease is yet to be answered. The fact that the comparison of pediatric IBD patients with controls, showed only little difference in enzyme expression suggests that children can possible compensate for defects.
Objectives and Study: Genetics plays a key role in the pathogenesis of inflammatory bowel disease (IBD). With the expanding use of next-generation sequencing, >100 different monogenic disorders directly causing IBD have been identified, and most of them present in the first years of life. Recently, several patients with severe IBD were identified to harbor pathogenic mutations in Receptor-interacting serine/threonine-protein kinase 1 (RIPK1) gene, which regulates necroptosis, a necrotic cell death mechanism. We present the clinical features, genetic analysis and immune work-up of three patients with infantile-onset IBD resulting from novel RIPK1 mutations.

Methods: Whole exome sequencing was performed in two patients with severe infantile-onset IBD, along with sanger sequencing for confirmation. Mass cytometry time of flight was conducted for in-depth immunophenotyping, including cytokine secretion analysis following lipopolysaccharide (LPS) or Phorbol myristate acetate with ionomycin (PMA-I), on one of the patient’s peripheral blood mononuclear cells, and compared to control subjects and patients with active Crohn’s disease.

Results: Both patients, born to consanguineous Muslim parents, presented with severe colitis and multiple perianal fistulas in the first months of life, and did not develop severe or atypical infections. One of the patients had a partial response to high doses of infliximab and azathioprine, while another one failed to respond to adalimumab and later to low dose anakinra, an IL-1 receptor antagonist. Genetic studies identified novel and pathogenic genetic variants in the RIPK1 gene in all patients, that were confirmed by Sanger sequencing. Immunoglobulin levels of these patients were within normal levels. Using mass cytometry time of flight unbiased clustering analysis, we identified peripheral immune dysregulation in one of these patients, characterized by an increase in IFNγ CD8+ T cells along with a decrease in monocytes, dendritic cells and B cells. Moreover, RIPK1-deficient patient’s immune cells exhibited decreased IL-6 production in response to LPS across multiple cell types including T cells B cells and innate immune cells.
Conclusions: Mutations in RIPK1 should be considered in very young patients presenting with colitis and perianal fistulas. Given RIPK1’s role in inflammasome activation, but also in epithelial cells, it is unclear whether IL1 blockade or allogeneic hematopoietic stem cell transplantation can suppress or cure the hyper-inflammatory response in these patients. Additional studies in humans are required to better define the role of RIPK1 in regulating intestinal immune responses, and how treatment can be optimized for patients with RIPK1 deficiency.
Feasibility of Using Real-World Data from the ImproveCareNow Registry to Examine the Efficacy of Ustekinumab for Paediatric Crohn’s Disease

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Objectives and Study: Significant unmet medical needs in paediatric patients with Crohn’s disease (CD) call for the use of real-world data (RWD) and real-world evidence (RWE) to enable faster access for paediatric patients to safe and effective therapies available to adults with CD. RWD collected during routine clinical practice has the potential to provide RWE to support the safety and efficacy of a paediatric drug approved in adults. This study evaluated the capability of the registry of the ImproveCareNow (ICN), the world’s largest paediatric inflammatory bowel disease (IBD) network, to generate relevant, reliable, high-quality RWE on the use of ustekinumab (UST) in paediatric CD.

Methods: We conducted a retrospective feasibility analysis of ICN registry data, including patients with CD treated with UST from January 2007 through July 2019. To determine the availability and completeness of data, counts and descriptive statistics were calculated for demographic and clinical characteristics (i.e., height, weight, biologic agents and corticosteroid use); laboratory tests (C-reactive protein [CRP], albumin, and hematocrit), ustekinumab dose and duration, and treatment efficacy, as measured by both short Paediatric Crohn’s Disease Activity Index (sPCDAI) and Physician Global Assessment (PGA).

Results: Since the approval of ustekinumab in adult CD in 2016, the use of UST in paediatric CD participants, though not an approved indication, has increased yearly. As of July 2019, a total of 692/738 (93.7%) ICN patients treated with UST had CD. At initial UST exposure, slightly more than half of CD patients were female (368; 53.2%), 419 (60.5%) were age 12 to ≤18 years old, 485 (71.7%) had ileocolonic disease, and 575 (83.1%) were previously treated with ≥1 biologic agent (Table 1). Overall, 576 patients (84.7%) weighed >40 kg and 104 patients (15.3%) weighed <40 kg at initial UST exposure. Of the 104 patients <40 kg, the majority (42; 79.2%) were 6 to <12 years old. For patients weighing >40 kg, the most common single intravenous induction doses ranged from 130 to 520 mg, but 81.3% received a maintenance dose of 90 mg subcutaneously every 8 weeks. The median (IQR) duration of UST exposure was 137 (0, 355) days. From baseline to 2 years of follow-up, among 1692 ICN patient visits reviewed, complete sPCDAI data were available for 70% of patient visits; 5 of the 6 sPCDAI variables were available for >90% of the visits. PGA was available for >95% of the visits. Height and weight-z scores, CRP, hematocrit, and albumin were available for 55% to 87% of the visits.
### Table 1

**Key characteristics of patients with a diagnosis of Crohn’s disease at the first ICN visit with a documented ustekinumab (UST) exposure in the registry between January 1, 2007 and July 31, 2019**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=692</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, N (%)</td>
<td>368 (53.2%)</td>
</tr>
<tr>
<td>White, N (%)</td>
<td>482 (85.5%)</td>
</tr>
<tr>
<td>Age (years) at initial UST exposure, N Mean (std deviation)</td>
<td>16.4 (3.14)</td>
</tr>
<tr>
<td>Age (years) at initial UST exposure, N (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;6</td>
<td>4 (0.6%)</td>
</tr>
<tr>
<td>6 to 12</td>
<td>53 (7.7%)</td>
</tr>
<tr>
<td>12 to 18</td>
<td>419 (60.5%)</td>
</tr>
<tr>
<td>≥18</td>
<td>216 (31.2%)</td>
</tr>
<tr>
<td>Weight, N (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;40 kg</td>
<td>104 (15.3%)</td>
</tr>
<tr>
<td>≥40 kg</td>
<td>576 (84.7%)</td>
</tr>
<tr>
<td>Missing</td>
<td>12</td>
</tr>
<tr>
<td>Number of days between the initial UST exposure and the latest UST administration, median (Interquartile range)</td>
<td>137 (0, 355)</td>
</tr>
<tr>
<td>Prior treatment with biologic agent, Yes, N (%)</td>
<td>575 (83.1%)</td>
</tr>
<tr>
<td>Corticosteroid use at UST initiation, Yes, N (%)</td>
<td>126 (18.2%)</td>
</tr>
<tr>
<td>Extent of disease at UST initiation, N (%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>10 (1.5%)</td>
</tr>
<tr>
<td>Ileal only</td>
<td>58 (8.6%)</td>
</tr>
<tr>
<td>Colonic only</td>
<td>115 (17.0%)</td>
</tr>
<tr>
<td>Ileocolonic</td>
<td>485 (71.7%)</td>
</tr>
</tbody>
</table>

**Conclusions:** This study demonstrated the feasibility, reliability, and completeness of ICN data as a potentially suitable source of RWE to evaluate the effectiveness of UST treatment in children with CD.

**Conflict of Interest:** S. Steiner, R. Colletti, R. Baldassano, S. Cohen, M.D. Kappelman and S. Saeed: investigators, advisors, and/or speakers for Janssen. E. King, S. Chen, and K. Olano: report nothing to disclose. R. Strauss, S. Volger and Y. Wang: are/were employees of Janssen Research & Development, LLC and own stock/stock options in Johnson & Johnson.
CD-TREAT diet induces remission and improves quality of life in an open label trial in children and adults with active Crohn’s disease.


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Objectives and Study: Exclusive enteral nutrition (EEN) is an established induction treatment for active Crohn’s disease (CD) with a proposed mechanism of action involving the gut microbiome. We have previously shown that CD-TREAT diet, a food-based diet with similar dietary profile to EEN, improves rat ileitis and replicates the effect of EEN on the gut microbiome of healthy volunteers and animal models. Here, we test the efficacy of CD-TREAT diet to induce clinical remission in active CD.

Methods: This is an open-label study in children (wPCDAI≥12.5) and adults (HBI≥5) with active CD. Primary outcome was clinical response (wPCDAI fall≥17.5; HBI fall≥3) or clinical remission (wPCDAI<12.5; HBI<5) after an 8-week treatment with CD-TREAT. Secondary outcomes included improvement of quality of life (QoL) and reduction in faecal calprotectin (FC) levels. Since CD-TREAT diet is gluten-free, adherence to treatment was assessed by the detection of the gluten immunogenic peptide (GIP) in faeces. Data are presented with median (IQR).

Results: 25 children, [age, 14.4 (12.5,15.7) years] and 32 adults, [age, 32.6 (24.2,43.9) years] were treated. 7 (12%) failed treatment and n=10 (18%) dropped out during the first 2 weeks of treatment due to palatability issues. In patients who completed 8 weeks of CD-TREAT course (n=40), 85% and 78% achieved clinical response and remission, respectively. CD-TREAT diet improved QoL in children [IMPACT-III score, baseline: 136 (122,143) vs 8weeks: 148 (133,153), p<0.01] and in adults [sIBDq score, baseline: 30 (26,45) vs 8weeks: 60 (48, 64), p<0.001]. Faecal GIP decreased during treatment [ng/g stool, baseline: 1250 (589, 1250), 4weeks: 0 (0,269), 8weeks: 0 (0,329), p<0.001 for both] showing adherence with the CD-TREAT diet. However, 33% and 40% of the patients had detectable faecal GIP at 4 and 8 weeks, respectively, revealing at least partial non-adherence. 30% of patients who completed CD-TREAT (n=12/40) experienced >50% FC reduction. Median FC levels decreased significantly in the group of patients (n=22) who had undetectable GIP at 4 and 8 weeks [mg/kg FC, baseline: 1190 (361,1129); 8weeks: 534 (92,1230), p<0.01].

Conclusions: CD-TREAT diet improved disease activity indices and QoL in the majority of patients who completed treatment and decreased FC in those who were most likely to be compliant. Future RCT should aim to compare CD-TREAT with other induction treatments and improve meal variety and palatability to improve compliance and reduce drop-out rates.
Validation of the simplified endoscopic mucosal assessment of Crohn’s disease (SEMA-CD): A novel endpoint to assess endoscopic improvement with real world data

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Objectives and Study: To demonstrate treatment efficacy in Crohn’s disease (CD), regulatory authorities require that trials include an endoscopic remission endpoint. However, standardized endoscopic assessment of mucosal improvement, such as the Simple Endoscopic Score of CD (SES-CD), is not typically recorded by clinicians in practice or outside of clinical trials. A previous study demonstrated the Simplified Endoscopic Mucosal Assessment of CD (SEMA-CD) correlates strongly with SES-CD and that SEMA-CD is a score that can be easily used by clinicians in routine practice (Adler et al., 2021). The objective of this current study was to validate the SEMA-CD scored colonoscopy videos in additional populations and to examine the reliability of SEMA-CD over a range of mucosal disease severity in paediatric and adult participants and to evaluate sensitivity to change over time.

Methods: We compared SEMA-CD and SES-CD scores in 110 patients with existing pre- and post-treatment colonoscopy videos from two ustekinumab clinical trials (UNISTAR, paediatric, n=36; SEAVUE, adult, n=74). Videos were separately scored with the SEMA-CD and SES-CD by professional central readers, blinded to video scores and to clinical history. Spearman’s rank correlation coefficient was used to evaluate correlation between scores, under different settings by study population (paediatric, adult), disease severity, and video quality. Inter- and intra-rater reliability were assessed with interclass correlation coefficient (ICC). Readers also rated ease of SEMA-CD scoring on a 7-point Likert scale.

Results: Most of the pediatric patients were ≥12 to <18 years old (75%) with a median (range) CD duration of 3.8 years (1-12 years). While 71.6% of the adult patients were ≥18 to <45 years in age with a median (range) CD duration of 3.4 years (0-40 years). More than half of the pediatric patients (60.0%) and adult patients (58.9%) had both ileal and colonic involvement. SEMA-CD was highly correlated (rho [95% CI]) with the SES-CD, 0.89 (0.86, 0.92; Figure 1). Pre-to post-treatment changes in SEMA-CD scores highly correlated with SES-CD scores (0.84 [0.77, 0.89]). The positive relationship remained strong between scores when comparing total scores in paediatric 0.94 (0.90, 0.96) and adult 0.86 (0.80, 0.89) participants; across SES-CD disease severity categories (inactive, mild, moderate, severe; rho range 0.69-0.85); and in “optimal” 0.90 (0.86, 0.93) and “less than optimal” quality videos 0.88 (0.83, 0.91). Intra- and inter-reader reliability (ICC [95%CI]) were high, 0.93 (0.88, 0.96) and 0.89 (0.85, 0.91), respectively. SEMA-CD was rated as the same as, or easier than SES-CD 99.6% of the time.
Conclusions: This study demonstrated the SEMA-CD is feasible, reliable, reproducible, and sensitive to change in both adult and paediatric patients with CD. SEMA-CD should serve as an easy score for clinicians to record mucosal improvement and provide quality real world evidence for research using data from clinical registries.

Conflict of Interest: Sheri Volger, Lenore Noonan, Laurie S. Conklin, and Kim Hung Lo are all employees of Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson) and own Johnson & Johnson stock and/or stock options. Richard B. Colletti has served in a consultancy/advisory role for Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson). Yongling Xiao is an employee of Cytel, Inc., Waltham, MA, USA, and has served in a consultancy/advisory role for Janssen Research & Development, LLC. Jeremy Adler has received research grants/funding from Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson).
The effect of exclusive enteral nutrition on inflammation related proteins in paediatric patients with crohn’s disease

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Objectives and Study: Exclusive enteral nutrition (EEN) is the recommended first line treatment for active paediatric Crohn’s disease (CD). The specific mechanism of action and immunological effects of EEN remain unclear. This study investigated the inflammation-related proteins in CD and ulcerative colitis (UC) patients, compared to non-inflammatory bowel disease (non-IBD) controls, and explored the effect of EEN in children with CD.

Methods: Children with active CD received EEN for around 8 weeks. Faecal and plasma samples were collected prior to EEN and upon EEN completion. Samples were also collected from paediatric UC patients and non-IBD controls. 92 inflammation-related proteins were quantified using the O’link Inflammation Panel. Faecal calprotectin (FC) was measured by ELISA. Patients in which FC decreased >50% during EEN were classed as FC responders; those with a <50% decrease in FC were classed as FC non-responders. Comparisons of inflammation-related protein levels across groups were performed using general linear model and Bonferroni comparisons. Significant differences are those with p<0.05.

Results: 84 patients were recruited (CD: 54, UC: 11, non-IBD: 19). Paired plasma samples were collected from 18 patients with CD receiving EEN. Of these, 72% achieved clinical remission by the end of EEN (wPCDAI <12.5). Compared to non-IBD controls, UC and CD patients prior to EEN had significantly different levels of 32 (29 raised, 3 lower) and 34 (31 raised, 3 lower) proteins, respectively. EEN led to significant changes of 24 proteins (18 increased, 6 decreased) compared to their baseline levels. All 6 proteins, CCL23, FGF-21, IL-24, IL-6, MMP-1, TGF-α, which decreased during EEN were significantly higher in patients with CD compared to non-IBD prior to EEN start. In patients classified as FC responders (n= 9) 22 proteins changed significantly during EEN; compared to 12 proteins in the FC non-responders (n= 7) group (Fig. 1). 17/22 (77%) of the proteins that changed significantly in the FC responder group during EEN, also changed during EEN in patients who entered clinical remission, including significant reductions in several inflammatory cytokines such as IL-6 and IL-8. Despite being higher in patients with CD prior to treatment than to non-IBD, 23 proteins, including IL-17A and oncostatin M, did not change in FC responders during EEN.
Conclusions: EEN treatment of CD alters the concentration of several inflammation-related proteins in plasma, including IL-6 and IL-8, consistent with the observed reduction in inflammation and improvement in clinical response. Surprisingly, some cytokines that have previously been associated with CD pathogenesis, including oncostatin M and IL-17A remain high in treated patients who achieved clinical remission.
Dual Biologic in Moderate to Severe Pediatric Inflammatory Bowel Disease: A Case Series.

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Objectives and Study: Pediatric inflammatory bowel diseases (PIBD) patients who qualify for the treatment in biological therapy represent a group with significant disease burden who have never succeeded conventional medication. Biologic agents are frequently used in the disease course, however they only result in 1-year remission rates of approximately 40% in given IBD populations. We aim to assess the efficacy and safety of concomitant use of 2 biologic therapies including: anti-TNF (infliximab, adalimumab) vedolizumab and ustekinumab in a refractory pediatric IBD cohort. We present our experience with combining dual biologic therapy in PIBD (a term mainly used to refer to Crohn’s disease (CD) and ulcerative colitis (UC)) between July 2021 and March 2022 in our Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, The Children’s Memorial Health Institute in Warsaw.

Methods: Ten children (6 ulcerative colitis, 1 ulcerative colitis/IBD-unspecified, 3 Crohn’s disease) with a disease duration of 3.5 (8mth-9) years, initiated dual therapy at an age of 11.6 (3–17) years after failing ≥2 biologic therapies. Five (50%) were treated with ustekinumab/adalimumab, 2 (20%) with vedolizumab/adalimumab and 3 (30%) with infliximab/vedolizumab. Disease activity (PUCAI and PCDAI scale) and fecal calprotectin were analyzed. Clinical remission was defined as a decrease in PCDAI of at least 12.5 points between baseline and 4 months after dose of a second biological drug for CD, and a decrease in PUCAI of at least 20 points between baseline and this time for UC.

Results: A clinical improvement was obtained in six children (60%; 2 UC, 1 UC/IBD-unspecified, 3 CD) in PCDAI/PUCAI scale after 4 months of dose a second biological drug. Clinical response in patients: mean baseline PCDAI score was 52.5 ± 6 and 7.5 ± 3 after induction therapy with second biological drug, while PUCAI score was 35 ± 20 vs. 5 ± 2, respectively. The median fecal calprotectin significantly decreased in patients who participated in the study for a minimum of 4 months from 1800 ug/g at baseline to 415 ug/g. Three patients (30%) did not improve on treatment. One patient improved significantly after 4 months of follow-up, but required a colectomy two months later (UC, vedolizumab/infliximab). In another patient, despite clinical improvement, dual biological therapy was discontinued due to an anal abscess (UC, vedolizumab/adalimumab). One patient died of cardiac complications after suffering from Covid infection (UC, vedolizumab/infliximab). We reported one adverse event during treatment in the form of an anal abscess.

Conclusions: In pediatric IBD, combining biological agents seems to be safe and beneficial in selected patients. The application of dual biological therapy seems to be an appealing therapeutic option and may bring a possibility to better tailor and customize the therapies for patients.
Objectives and Study: Crohn’s disease (CD) causes chronic progressive bowel damage if not well controlled. Monoclonal and small molecule medications (called here biologics) have dramatically improved CD outcomes. However, few biologics are available, and some patients discontinue one biologic after another, sometimes exhausting available biologics before reaching adulthood. It is not known how often loss of biologic options may be preventable. We conducted a multicentre study to determine patterns of biologic use, discontinuation, and evaluations prior to discontinuation.

Methods: We identified all patients with CD at 7 Paediatric Inflammatory Bowel Disease Centres in the US (2010-2021) via the ImproveCareNow (ICN) Network registry. Inclusion required enrolment in ICN <30 days after diagnosis and age at diagnosis <18 yr. Medical record abstraction supplemented prospectively collected ICN registry data. Patient characteristics, treatments, reasons for and evaluations prior to biologic discontinuation were classified. Therapeutic drug monitoring (TDM) was considered proactive if done during quiescent disease. Induction TDM was 12-16 weeks after 1st dose. Changes in biologics were visualized with Alluvial plots (RawGraphs 2.0). Bivariate comparisons were performed using chi-square (Stata 17.0). The study was approved by each institution’s Institutional Review Board.

Results: Data from 400 patients were analysed to date. In total, 345 (86%) started a biologic (83% infliximab, 16% adalimumab, 1% ustekinumab, <1% vedolizumab), among whom, 107 (31%) eventually discontinued it. During treatment with their 1st biologic, TDM was performed during induction for 142 (41%), and at any time during treatment for 288 (83%). Most TDM (74%) was proactive. Discontinuation of the 1st biologic was less likely if induction TDM was performed (25% vs 36%, p=0.028). Discontinuation was also less likely if proactive TDM was ever performed (26%) compared to only reactive TDM (63%) or no TDM (37%; p<0.001).

Among those who discontinued the 1st biologic, reasons included primary non-response (11%), secondary loss of response (33%), development of anti-drug antibodies (7%), adverse event (25%; 3 considered serious), non-adherence or choice (9%), and health insurance problems (4%). Among discontinuers due to inadequate efficacy (N=47), 91% underwent at least some pre-discontinuation evaluation, including checking level/antibodies (79%), faecal calprotectin (19%), endoscopy (38%), or imaging (52%). After discontinuing the 1st biologic, 98 (91%) switched to a 2nd biologic, and 9 (8%) discontinued without starting another biologic. Of all on 2nd biologic, 21% switched to a 3rd biologic, among whom 21% switched to a 4th biologic. Of all biologic starters, 33 (9%) went on to a 3rd or 4th biologic during paediatric care (Figure 1).
Changes in medication use. Those who never changed remain in the same category.

Conclusions: In this multicentre study of paediatric CD, we found 30% of those who started a 1st biologic eventually discontinued it, and 20% discontinued each subsequent biologic. In all, 9% used multiple biologics. Proactive TDM may reduce risk of biologic discontinuation. From these data 37% fewer may have discontinued if proactive TDM was conducted. Strategies are needed to preserve biologic efficacy, improve treatment outcomes, and prevent loss of treatment options.
The musculoskeletal manifestations of paediatric inflammatory bowel disease (IBD): the GOSH experience

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Objectives and Study: Children with Inflammatory bowel disease (IBD) have extra-intestinal manifestations. Musculoskeletal (MSK) manifestations are known to be the most common extra-intestinal manifestations of IBD. Though it is well described that IBD can have systemic manifestations, the exact mechanism of joint disease and its relation to intestinal disease is still unclear. Patient and disease characteristics, treatments, and outcomes of paediatric IBD-associated MSK disease are not well established. This study aims to describe the MSK manifestations seen in children with IBD.

Methods: A retrospective cohort study was carried out between February 2011 and May 2022 looking for all children with IBD who presented at any time of their disease with inflammatory MSK manifestations (chronic arthritis or chronic non-infectious osteomyelitis) (CRMO) at Great Ormond Street Hospital for children. All patients presented with MSK pain and have no clinical or radiological evidence of inflammatory MSK involvement were excluded from the study.

Results: Out of the 795 patients with IBD, twenty-four patients (3.1%) were found to have inflammatory arthropathy. However, 114 patients were referred to rheumatology with MSK pain. Median age at diagnosis of MSK manifestations was ten years. Most of the patients were male (66.7%) and had Crohn’s disease (19/24). 21 patients had chronic arthritis, 9 patients (42.9%) had axial arthritis and 12 patients (57.1%) had peripheral arthritis. Six patients had chronic non-infectious osteomyelitis (CNO). Three patients had both.

21 patients had confirmed chronic arthritis or CNO on imaging. A further 2 patients had clinical florid peripheral arthritis. Eight patients had ultrasound findings: arthritis and tenosynovitis. 20 patients had MRI changes (on focal or WB-MRI): Bone marrow oedema, enthesitis, synovitis and bone erosions. There was a positive family history in 5 patients (20.8%): mostly IBD.

Seven patients (29.2%) were found to have skin manifestations mostly described as psoriasis (3/7) and Keratosis Pilaris (2/7). Twenty-three patients (95.8%) had constitutional symptoms. Twenty-one patients (87.5%) had raised inflammatory markers. Seven patients were ANA positive, 2 patients Rheumatoid factor positive and 3 patients HLA-B27 positive.

Six patient received enteral feeds, 19 azathioprine and 5 sulfasalazine. 17/24 patients were treated with biologics. Anti-TNF was the most used biologics (infliximab was used in 13 patients and adalimumab was used 9 patients). Ustekinumab was used in 4 patients only. There was a statistically significant positive correlation between age of diagnosis of IBD and age of diagnosis of arthropathy (r= 0.593, P= 0.002), suggesting that they occur at the same age. There was no statistically significant association between IBD remission and arthropathy remission (Fisher’s exact, P= 0.082).

Conclusions: This study describes the inflammatory MSK manifestations (chronic arthritis and CNO) of children with IBD. A significant number of children with IBD have MSK pain but their clinical and or radiological findings did not support the diagnosis of inflammatory arthropathies. This may be explained by missing subtle arthritis/enthesitis radiologically or the presence of biomechanical pain. Larger studies are needed to identify predictors of outcome in children with MSK manifestations of IBD.
P-030

Patient-Reported-Outcome-Measurement Information System (PROMIS) in Paediatric Inflammatory Bowel Disease- Preliminary study of clinical usefulness

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Objectives and Study: Patient-reported outcomes (PROs) are measures of treatment outcome and disease management that are reported by the patient and/or caregivers. Patient-Reported-Outcome-Measurement Information System (PROMIS), was developed to address, investigate, and promote the use of PROs among patients with chronic conditions. PROMIS instruments are calibrated using a T-score metric with the mean of the original calibration population equal to 50. Paediatric Inflammatory Bowel Disease (IBD) is an interesting model of relapsing chronic disease for PROMIS application and data are emerging but not yet in the real clinical setting. This study aims to evaluate the potential, real life, clinical usefulness, and responsiveness of selected PROMIS measures by comparing them with objective clinical data and validated Quality of life (QoL) scores (IMPACT-III) in a cohort of paediatric Crohn’s disease (CD) patients.

Methods: Prospective and cross-sectional study. Data collected since January 2021. Paediatric CD aged 8-17 years, in outpatient setting were included. Preliminary results are presented: baseline (T0) and 6 months follow-up (T1). Comparison of 10 short form paediatric PROMIS measures (global health, meaning and purpose, cognitive function, life satisfaction, peer relationship, depression, anxiety, pain interference, physical activity, fatigue) with Paediatric Crohn’s disease activity index (PCDAI), laboratory and endoscopic parameters and IMPACT III. Sub analysis of 2 groups: remission (G1) and active disease (G2).

Results: 31 patients included (58%Female); mean age:15,4y (±2) mean age at diagnose 12,7y(±3,4), Phenotype :77,4%A1b; 58%B3; 87%B1; 22,6%p; 87%G0; Sub groups: G1 (TO/T1) :22/23; G2 (T0/T1):9/8.

At T0, comparing G1 with G2: mean PROMIS score reflected better physical, emotional and social health: PROMIS global health 43,6/35,3, meaning and purpose 40,1/34,4, cognitive function 44,9/43,3, life satisfaction 44,3 /36,6, peer relationship 50,1/43,6, depression 45,5/56,6, anxiety 46,5/51,5, pain interference 41,1/53,4, physical activity 40,4/42,3, fatigue 48,3/54,2. This was associated (p<0,005) with mean score of PCDAI (3,4/15), IMPACT III (74,9/57), SES-CD (5/15,7), calprotectin (426,8/615,9) and Haemoglobin (12,8/11,1g/dl), blood sedimentation rate (16,9/28,5 mm) e C-reactive protein (0,3/1,5 mg/dl).

Also in T0: PROMIS global health r= 0,55, meaning and purpose r= 0,53, cognitive function r= 0,49, life satisfaction r= 0,68 and peer relationship r= 0,44 were positively correlated with IMPACT-III (p<0,001); PROMIS depression r=-0,74, anxiety r = -0,66, pain interference r= -0,49, and fatigue r= - 0, 50 were negatively correlated (p<0,001) with IMPACT III. A weaker correlation was found whit other data. Comparing T0 and T1 results: better mean IMPACT-III score (73 /77,2) was found at T1. Furthermore, the same correlations with PROMIS and IMPACT III were found.

Conclusions: This preliminary data is in accordance with the recent evidence, reporting that PROMIS have the ability of reflecting the disease activity in different points of time. In this study, however, a strong correlation was only found with QoL. Our current ongoing study may disclose stronger correlation with conventional assessment instruments used in clinical setting to monitor paediatric CD.
P-031 (Poster of distinction)

Letting Go of Control: Experience and Involvement of Parents of Young Adults with Inflammatory Bowel Disease Transitioning from Paediatric to Adult Care

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Objectives and Study: A paediatric diagnosis of inflammatory bowel disease (IBD) represents a major event for a family - one with psychological, socioeconomic, and behavioural impacts. Parents typically become active participants in their child’s care by arranging appointments and medication refills, while managing financial and emotional challenges associated with chronic disease. As their child transitions from paediatric to adult care, parents need to step back and allow their child to take responsibility for disease management. This study aimed to understand the experience of parents whose child with IBD has transitioned from paediatric to adult care. To achieve this aim, the study objectives were to describe parents’ feelings surrounding their child’s transition and their level of involvement in adult care.

Methods: Parents from the province of Alberta, Canada were recruited by patient referral for semi-structured interviews. Inclusion criteria were having a child with IBD who transitioned to adult care from 2018-2020, who were diagnosed for at least a year prior to transitioning, and participated in previous interviews that examined perspectives on transition. Interviews were transcribed verbatim and then analyzed by latent context analysis. This study used a naturalistic inquiry approach with the method of qualitative description.

Results: We conducted 13 semi-structured interviews to achieve thematic saturation. A summary of characteristics of parents who participated is in Table 1. Main themes related to feelings around their child’s transition were sadness (n=5) and fear (n=7), while two parents mentioned neutral feelings. Most parents were involved in their child’s adult care through disease management (n=11), where five parents only attended the first appointment in adult care and the remaining six managed their child’s care through attending and making appointments, communicating on their behalf, and obtaining medications. Logistics of care (n=6) was characterized in part by driving their child to appointments and obtaining all health information directly; and indirect involvement (n=7), which included acting as a support system for their child, engaging in discussions about care, while encouraging and guiding when needed. The theme of parent feelings explained why parents were involved in care (n=5) and was characterized by feeling that their job as a parent was to protect and help their child, feeling guilty, and that being involved was easier. Another theme was child’s circumstances (n=4), characterized by the belief that their child was too busy with friends and school, and that their child was not proactive, organized, or responsible.
Conclusions: The results suggest that most parents experience negative feelings relating to their child with IBD transitioning from paediatric to adult care. Parents were involved in their child’s care both actively and indirectly. Reasons for involvement varied from parents’ personal feelings to comments on their child’s circumstances. Through understanding parents’ experiences during transition, targeted interventions can be implemented that addresses parental emotions involved in the transition process, and ultimately supporting parents to transfer responsibility of disease management to the child.

Table 1. Demographics of parents who participated in semi-structured interviews

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Total N</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parents</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td><strong>Relationship to Patient</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>13 (100)</td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Child Living Situation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lives with parent</td>
<td>5 (38.5)</td>
<td></td>
</tr>
<tr>
<td>Does not live with parent</td>
<td>8 (61.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Highest Education Level Attained</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>5 (38.5)</td>
<td></td>
</tr>
<tr>
<td>Certificate</td>
<td>2 (15.4)</td>
<td></td>
</tr>
<tr>
<td>Diploma or undergraduate degree</td>
<td>5 (38.5)</td>
<td></td>
</tr>
<tr>
<td>Master’s degree</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex of Child</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>8 (61.5)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5 (38.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Number of Other Children</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3 (23.1)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>7 (53.8)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3 (23.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Occupation Field</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administrative, business, finance, and management</td>
<td>6 (46.2)</td>
<td></td>
</tr>
<tr>
<td>Entertainment</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td>Health</td>
<td>2 (15.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Other:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IT service dispatcher</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td>Stay at home mom</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td>Long term disability</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td>Day home provider</td>
<td>1 (7.7)</td>
<td></td>
</tr>
</tbody>
</table>
Predicting Transition Success in Young Adults with Inflammatory Bowel Disease: a Single Site Retrospective Cohort Study

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Objectives and Study: Individuals diagnosed with inflammatory bowel disease (IBD) in childhood present more often with extensive disease, are more likely to be admitted to hospital and are less adherent with clinic appointments. In Canada, approximately 25% of IBD patients are diagnosed in childhood and the incidence of childhood IBD diagnoses is increasing; therefore, a smooth, uninterrupted transition from paediatric to adult care should be a priority. Previously, we conducted interviews with providers, patients, and parents on their perspectives on what defines successful transition. Themes that emerged included independence in seeking care and disease management. Our current objective is to investigate whether indicators of success identified in our previous research can be used to predict which patients are more likely to successful transition from paediatric to adult care. To achieve this objective, this study aims to identify patient characteristics associated with the frequency of successful transition.

Methods: We conducted a retrospective cohort study using electronic medical charts to obtain data on IBD patients who transitioned to adult care from 2014 –2019 at an IBD clinic in Alberta, Canada. A literature review was conducted by AB to identify variables reported to be predictors of transition success for other chronic diseases. We abstracted potential predictors, including whether parents were divorced, cigarette use, medication nonadherence, biologic use, and age at diagnosis. These were abstracted at first adult appointment, when notes on paediatric history are typically recorded. We chose available success indicators related to two themes: independence in seeking care (e.g., attending appointments) and disease management (e.g., stable therapy and medication adherence). We abstracted success indicators within a two-year period from first appointment in adult care. In a preliminary analysis, we used logistic regression to estimate unadjusted odds ratios (OR) for the association of potential predictors with success indicators. Subsequent analysis will use multivariable regression modelling to estimate risk differences.

Results: We reviewed medical charts of 145 patients. At first adult appointment, the median age at diagnosis was 14.4 years (IQR: 13.1 – 15.9); 57% of patients were on biologic agents. Within two years from first adult appointment, 17% of patients required either a therapy initiation onto a biologic or a change in biologic, 25% had at least two instances when parents called on their behalf, and 15% had medication nonadherence noted. For potential predictors of medication nonadherence in adult care, regression analysis (Table 1) estimated strong associations with paediatric medication nonadherence (OR~15) and younger age at diagnosis (OR~14). For potential predictors of not showing up to an adult appointment, strong associations were estimated for having divorced parents (OR~6.6) and daily cigarette consumption (OR~10). Potential risk factors for requiring a change in therapy included not being on a biologic therapy at the time of transition and having a history of medication non-adherence in pediatric care.
Table 1: Estimated associations of potential predictor variables measured at time of first adult appointment with transition success indicators ascertained in two years of follow-up after first appointment in adult care.

<table>
<thead>
<tr>
<th>Predictor Variables *</th>
<th>Appointment No Show OR (95% CI)</th>
<th>Change in Therapy OR (95% CI)</th>
<th>Medication Nonadherence OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divorced Parents (yes, no)</td>
<td>OR: 6.6 (1.5,29)</td>
<td>N/A</td>
<td>OR: 7.2 (1.4,39)</td>
</tr>
<tr>
<td>Not on a biologic therapy</td>
<td>N/A</td>
<td>OR:2.8 (1.3,6.1)</td>
<td>N/A</td>
</tr>
<tr>
<td>Daily cigarette Use (any, none)</td>
<td>OR:10 (1.9,57)</td>
<td>N/A</td>
<td>OR: 4.2 (0.8,22)</td>
</tr>
<tr>
<td>Nonadherence in pediatric care (any, none)</td>
<td>OR:3.3 (0.8,13)</td>
<td>OR:2.8 (1.1,7.0)</td>
<td>OR: 15 (3.7,63)</td>
</tr>
<tr>
<td>Age at diagnosis (0-10 years, 14-17 years)</td>
<td>OR: 0.3? (0.0, 3.5)</td>
<td>N/A</td>
<td>OR: 14 (2.0,90)</td>
</tr>
</tbody>
</table>

OR, Odds Ratio; CI, Confidence Interval

Conclusions: These preliminary results identified potential predictors of transition success when defined as adhering to appointments and medication, and to a lesser extent when defined as change in therapy.
Effective treatment with Ustekinumab in a 3-year-old with chronic granulomatous disease-related colitis: a case report

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Objectives and Study: Chronic granulomatous disease (CGD) is an inborn error of immunity caused by nicotinamide adenine dinucleotide phosphate (NADPH) oxidase deficiency. Due to impairment of reactive superoxide anion and metabolite formation, those affected are at high risk of bacterial and fungal infections and require antimicrobial prophylaxis. Dysregulated inflammation may cause CGD-associated inflammatory bowel disease or CGD colitis, the management of which can be challenging. Anti-TNF therapies are relatively contraindicated due to high frequency of serious and invasive infections. Ustekinumab, a monoclonal antibody inhibiting interleukin-12 and -23 is an efficient second-line biologic treatment for Crohn’s Disease. Here we describe the effective treatment of a 3 year-old child with CGD colitis with Ustekinumab.

Methods: The female patient was prenatally diagnosed with autosomal recessive p47 CGD following screening in view of family history. She had a homozygous pathogenic variant in NCF1 (c.75_76delGT). She was put on antimicrobial prophylaxis shortly after birth and had not experienced significant infectious or gastrointestinal complications prior to prior to matched sibling donor haematopoietic stem cell transplant (HSCT) at the age of 2 years and 9 months. 5 months post-HSCT she developed chronic diarrhoea in the context of decreasing myeloid engraftment (to 15%) despite satisfactory lymphoid engraftment. Abdominal ultrasound suggested a long segment of colonic inflammation from hepatic flexure to the sigmoid. Infectious causes were excluded using conventional and molecular approaches. Oesophago-gastro-duodenoscopy and colonoscopy were performed. Macroscopically, severe pancolitis was evident, with a histological picture suggesting a degree of Graft-versus-Host-Disease superimposed on a severe mixed inflammatory process with acute and chronic features felt most likely to be driven by the underlying CGD-related immune dysregulation. Gut rest with parenteral nutrition and high dose IV steroids improved stool output but did not result in sustained weight gain or improvement in inflammatory markers. Ustekinumab was initiated, preferred to anti-TNFs in view of infection-related safety concerns with the latter, and mindful of the potentially faster onset of action compared to vedolizumab.

Results: There was a rapid and dramatic response to Ustekinumab. Within 6 weeks after the intravenous loading dose, stool output was normal on full enteral nutrition, intravenous steroids were able to be effectively weaned and stopped, and she was well enough to be discharged from hospital. There was a significant and sustained improvement in weight and key laboratory indices (Figure 1). Faecal calprotectin levels of 1620 ug/g prior to Ustekinumab normalised within one month to <30 ug/g and no bowel thickening was identified in an ultrasound at that time (Figure 1).
**Conclusions**: Ustekinumab was effective rescue treatment in a child with CGD colitis not responding to high-dose IV steroids and gut rest. To our knowledge this is the youngest reported patient with CGD colitis treated with Ustekinumab. The clear evidence of efficacy prioritises Ustekinumab for consideration in similar cases of CGD colitis not responding to conventional treatment approaches.
P-034

Sugar Intestinal Permeability Test correlates with paediatric Crohn’s disease phenotype and activity and predicts the development of a stricturing behaviour

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Objectives and Study: Increasing evidence supports the central role of intestinal barrier dysfunction in the pathogenesis of inflammatory bowel disorders (IBD). Sugar intestinal permeability test (SIPT) is a useful, non-invasive method to assess intestinal permeability (IP). Few studies have evaluated the clinical implication of impaired IP and the potential role of SIPT in paediatric IBD.

This study aims to evaluate: 1) The degree of IP impairment in paediatric IBD at diagnosis and within different IBD types; 2) The relationship between IP and other markers of disease activity, in order to evaluate the potential role of SIPT in Crohn’s disease (CD) follow up; 3) The prognostic implication of impaired IP in the development of CD complications and need for surgery.

Methods: A monocentric, retrospective, observational study was performed. We included children with an established diagnosis of IBD who performed at least one SIPT with lactulose and mannitol between January 2010 and July 2021, either at IBD diagnosis or during follow-up. SIPT results were compared to clinical, radiological, endoscopic, and histologic disease parameters, inflammatory indexes, growth parameters and disease location.

Results: Aim 1. 84 children (M 52%, median age 12 years) underwent SIPT at IBD diagnosis (55 with CD, 18 with Ulcerative Colitis [UC], and 11 with unclassified IBD [IBD-U]). An alteration of IP was observed in 87.3% of CD, in 38.9% of UC and in 63.6% of IBD-U. The lactulose/mannitol ratio (LMR) was significantly higher in children with CD compared to those with UC (p 0.0004). The LMR showed a good accuracy in discriminating between children with CD and other IBD sub-types (ROC curve: AUC 0.75; 95% CI: 0.65 – 0.87), the most accurate cut-off of LMR being 0.05 (67% sensitivity, 79% specificity).

Aim 2. 136 SIPT were performed in 71 CD patients (M 50.7%, median age 13 years), either at diagnosis or during follow up. LMR positively correlated with markers of CD activity: PCDAI clinical score, CRP, ESR, faecal calprotectin, and SES-CD endoscopic activity score (p <0.0001). LMR was significantly higher in patients with histologic signs of active CD compared to those with histologic remission. LMR showed a good accuracy in identifying patients with histologic CD activity (ROC curve: AUC 0.76; 95% CI: 0.65 – 0.88). A LMR cut-off of 0.03 resulted as the most accurate in identifying patients with active CD (72% sensitivity, 68% specificity).

Aim 3. The outcome of 53 CD patients (M 56.6%, median age 12 years) who underwent SIPT at CD diagnosis was assessed (median length of follow up 5.2 years): 8 patients required abdominal surgery, 11 developed perianal disease, 15 a stricturing phenotype, 5 a penetrating disease. An increased urinary excretion of lactulose at diagnosis predicted the development of a stricturing phenotype in the logistic regression analysis (p 0,02; OR 2.25 95% CI: 1.09 – 4.66).

Conclusions: Alterations of IP are highly prevalent in children with IBD. The SIPT proved to be a useful non-invasive tool to discriminate CD among the other IBD types at diagnosis, to detect luminal inflammation during follow up, and to predict the risk of developing a stricturing phenotype over time. Further studies are needed to confirm these results prospectively in a broader cohort of children diagnosed with IBD.
P-035

De-escalation of anti-tumour necrosis factor agents and reduction of adverse effects: a systematic review

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Objectives and Study: Long-term use of anti-tumour necrosis factor (TNF) agents can lead to adverse effects, such as infections and immune-mediated cutaneous reactions. Whether de-escalation by dose reduction or interval lengthening reduces these adverse effects is uncertain. This systematic review aims to compare the incidence of infections and skin manifestations after anti-TNF dose de-escalation with standard dosing.

Methods: MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials were searched from inception to January 14, 2022. Randomized controlled trials (RCTs) and observational studies comparing anti-TNF de-escalation strategies with standard dosing among patients with inflammatory conditions, that report on infections, skin manifestations or both were included. Risk of bias was assessed with the revised Cochrane risk-of-bias tool (RCTs) or the Newcastle-Ottawa Scale (non-RCTs).

Results: 14 RCTs and 6 observational studies (or 2706 patients) were included. Eight RCTs had low risk of bias or some concerns. Four non-RCTs were of good methodological quality. The studies described patients with axial spondyloarthritis (8 studies, 780 patients), rheumatoid arthritis (7 studies, 1458 patients), psoriasis (3 studies, 332 patients), or inflammatory bowel disease (2 studies, 136 patients). De-escalation strategies included interval lengthening (12 studies, 1317 patients), dose reduction (6 studies, 1130 patients) or both (2 studies, 259 patients). Overall, the occurrence of infections and skin manifestations did not differ between standard treatment and de-escalation, but most studies were underpowered to detect a potential difference. Disappearance of infections or skin manifestations after de-escalation was only reported in two studies. The majority of studies focused on etanercept and adalimumab. Heterogeneity in reporting of infections and skin manifestations precluded meta-analysis.

Conclusions: We found that anti-TNF de-escalation does not reduce infections or skin reactions, but the level of evidence is low. A de-escalation strategy should not be recommended for the sole purpose of reducing drug-related adverse effects. Meticulous documentation of adverse effects is recommended to further address this question.
P-036 (Poster of distinction)

Post-vaccination immunogenicity of BNT162b2 SARS-CoV-2 vaccine and its predictors in pediatric patients with inflammatory bowel disease

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Objectives and Study: Vaccination by mRNA BNT162b2 SARS-CoV-2 vaccine in children over 12 years old commenced in our country in July 2021. We prospectively compared the post-vaccination immunity of our pediatric patients with inflammatory bowel disease to that of healthy controls and looked for predictors of its robustness.

Methods: Anti-receptor binding domain, anti-spike S2, and anti-nucleocapsid immunoglobin-G and immunoglobin-A levels were measured in 139 pediatric patients with inflammatory bowel disease (65 vaccinated, median age 16.3, IQR 15.2–17.8y) and 1,744 controls (46, 37–57y) using microblot array.

Results: All inflammatory bowel disease and control patients developed positive anti-receptor binding domain immunoglobin-G antibodies at comparable titers. The proportion of observations with positive anti-spike S2 immunoglobin-G was higher in patients with inflammatory bowel disease than in controls (63% vs. 21%, OR 2.99 [1.51–5.90]), as was its titer (median (IQR) 485 [92–922] vs. 79 [33–180] IU/mL). Anti-receptor binding domain and anti-Spike S2 immunoglobin-G levels were associated with IBD status. We found an association between anti-spike S2 immunoglobin-G levels and time since vaccination (beta -4.85,95%CI -7.14–2.71,p=0.0001), history of SARS-CoV-2 PCR positivity (206.76,95%CI 39.93–374.05,p=0.0213), and anti-tumor necrotizing factor treatment (-239.68,95%CI -396.44–83.55,p=0.0047). Forty-three percent of patients reported vaccination side effects (mostly mild). Forty-six percent of observations with positive anti-nucleocapsid immunoglobin-G had a history of SARS-CoV-2 infection.

Conclusions: Patients with inflammatory bowel disease produced higher levels of post-vaccination anti-Spike S2 antibodies than controls. Previous SARS-CoV-2 infection is associated with higher and anti-tumor necrotizing factor treatment with lower production of post-vaccination antibodies.

Biologic Response and Remission in Paediatric-Onset and Adult-Onset Inflammatory Bowel Disease


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Objectives and Study: Extrapolation of efficacy from adults can reduce the number of children required to participate in clinical trials, but data must support the assumption of similar therapeutic response in paediatric and adult inflammatory bowel disease (IBD). We aimed to explore whether response to treatment is similar between paediatric and adult-onset IBD.

Methods: Data from 11 randomized, double-blind, placebo-controlled adult phase 2 and 3 trials of 4 biologics were analyzed. Participants were categorized as having adult- or paediatric-onset disease (<18 or ≥18 years). Multivariable modelling explored the association between age at onset and response to treatment after adjustment to disease duration, extent, and severity at baseline.

Results: Data from 6,283 study participants (2,575 with Crohn’s disease [CD], 3,708 with ulcerative colitis [UC]) were evaluated. Of 2,575 participants in CD trials, 325 were <18 years old at diagnosis; 836 participants (32.4%) were receiving placebo, while 1,739 were receiving active treatment. Of 3,708 participants in UC trials, 221 were <18 years old at diagnosis; 1,212 (33%) were receiving placebo, while 2,496 were receiving active treatment. Data from dose arms were pooled, as the purpose was to evaluate similarity of therapeutic response between paediatric and adult onset IBD within the same trial (not between doses or across trials). Graphs will be presented showing the proportion of participants in response in each trial, adjusted for disease duration and baseline clinical score (and for UC, extent of disease), including placebo and combined dose treatment groups. Odds ratios for response and remission were similar for paediatric-onset and adult-onset participants, before and after regression analysis, with overlapping confidence intervals.

Conclusions: Data presented here provide support for the assumptions underlying extrapolation of efficacy of biologics from adults to children with IBD.

Conflict of Interest: KHL, LK, SV, RZ, RS, RN and LSC: Employed by Janssen and have ownership interest (stocks and/or stock options) JRR: Grant/research funding: Abbvie, Janssen; Consultant/advisor: Abbvie, Bristol-Myers Squibb, Janssen, Eli Lilly, Pfizer AMG: Consultant: Abbvie, Amgen, Bristol-Myers Squibb, Janssen, Lilly, Merck, Pfizer, Sorriso; Speaker fees: Abbvie, Janssen, Nestle; investigator-initiated research support from Abbvie JSH: Consultant: Janssen, Bristol Myers Squibb, Boehringer Ingelheim, Takeda, Thetis, Lilly, Pfizer DT: (last 3 years) Consultation fee, research grant, royalties, or honoraria: Janssen, Pfizer, Ferring, Abbvie, Takeda, Atlantic Health, Shire, Celgene, Lilly, Roche, ThermoFisher, BMS MD: Consultation fee: Abbvie, Arena Pharmaceuticals, Boehringer Ingelheim International GmbH, Bristol-Meyers Squibb, Celgene, Eli Lilly, Hoffman-LaRoche, Genentech, Prometheus Biosciences, Takeda, UCB; Contracted Research: AbbVie, Janssen, Pfizer, and Prometheus; Ownership interest: Trellus Health Inc; Licensing fee: Takeda SAC: Research support: Abbvie, Janssen, Lilly, Takeda, BMS, Kate Farms, Arena. Consultation fees from Janssen, Kate Farms
P-038 (Poster of distinction)

Epidemiology of Venous Thromboembolism in Paediatric-Onset Inflammatory Bowel Disease: A nationwide population-based study in Korea

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Objectives and Study: Venous thromboembolism (VTE) is an important life-threatening complication of inflammatory bowel disease (IBD), and its risk is higher in IBD patients than in the general population. However, research on paediatric-onset inflammatory bowel disease (PIBD) is limited. We investigated the incidence of VTE in PIBD patients and compared them with adult IBD patients using nationwide population-based data in South Korea.

Methods: Healthcare data were extracted and processed from the National Health Insurance Sharing Service (NHISS) for a period of 13 years from 2005 to 2017. We used the AMC algorithm for Korean IBD big data (AKIB), which we previously created. According to the Paris classification of IBD, a child diagnosed with IBD under 17 years of age (A1 group) was defined as having PIBD. Pulmonary embolism, deep vein thrombosis, cerebral venous thrombosis, retinal vein thrombosis, and other venous embolism and thrombosis were included in VTE. Additionally, VTE patients were included in the study when the VTE code was entered later than the diagnosis of IBD. We analysed and compared the incidence of VTE between children and adults, Crohn’s Disease (CD) and Ulcerative Colitis (UC), and between males and females using a chi-square test and multivariable logistic regression.

Results: A total of 40,914 IBD patients (CD 14,290, UC 26,624) were included: 37,936 adults (CD 12,202, UC 25,734) and 2,978 children (CD 2,088, UC 890). Throughout all ages, 278 out of 14,290 CD patients [1.9%] and 1,014 out of 26,624 UC patients [3.8%] were diagnosed with VTE (P<0.001). Among children, 11 out of 2,088 CD patients [0.5%] and 13 out of 890 UC patients [1.5%] were diagnosed with VTE (P=0.009). The incidence rates of VTE were 47.8 (45.23–50.48) for total IBD, 30.98 (27.44–34.84) for CD and 56.16 (52.76–59.73) per 10,000 person-years (PY) for UC. In PIBD, 13.43 (8.6–19.98) for total, 8.99 (4.49–16.08) for CD and 23.07 (12.28–39.45) per 10,000 PY for UC. Adults, females, and UC were associated with an increased risk of VTE on multivariable analysis (Adults: adjusted odds ratio [aOR], 3.41; 95% confidence interval [CI], 2.27–5.14, females: aOR, 1.23, 95% CI, 1.10–1.37, UC: aOR, 1.78; 95% CI, 1.55–2.04). Other incidence rates are described in the figure.
**Conclusions**: This nationwide population-based study showed general information about VTE incidence in Korean IBD patients. VTE occurred less frequently in PIBD than in adult IBD. Also, VTE incidence was higher in females and UC.
Surgery’s role in paediatrics inflammatory bowel disease: our 12-years’ experience


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Objectives and Study: Despite recent advances in medical treatment in Inflammatory Bowel Disease (IBD), surgery still takes a relevant role in its management. We aimed to evaluate the subset of paediatric IBD patients that were submitted to surgery.

Methods: We performed a retrospective descriptive analysis of the clinical records of patients diagnosed between April 2010 and April 2022 in current follow-up at the Paediatric Gastroenterology Unit of a tertiary paediatric hospital, with special focus on those who underwent surgical intervention and its post-operative results.

Results: 99 patients with IBD were included, in which most had Crohn’s Disease (CD) (69.7%), followed by Ulcerative Colitis (UC) (21.2%) and Unclassified Colitis (UnC) (9.1%), with a predominance of males (62.6%). The median age at diagnosis was 13 years (IQR: 11-15) and the median duration of follow-up was 31 months (IQR: 11-51).

Of those, 11 patients (11,1%) were proposed to surgery: 9 with CD, 1 with UC and 1 with UnC, making up to 17 surgeries. From those with CD, 3 were submitted to ileocecectomy due to stenosing and fistulizing distal ileal disease. The other 6 had fistulizing perianal disease: the first had 4 surgeries to his complex perianal fistula prior to diagnosis and 4 others had perianal abscesses’ drainage (3, 4, 5 and 60 months after CD diagnose). 2 patients had a seton placed. The UC patient had a colic perforation at presentation and was interventioned before referral to our centre. At last, the UnC had an ileostomy performed in the first year of life in a European reference centre.

Conclusions: Approximately 10% of our IBD patients needed surgical intervention with a broad of clinical challenges. However, perianal disease embodies an important pathology as it represents more than half of all surgical procedures in our group. Paediatric IBD and its complexity demands a close collaboration between paediatric gastroenterologists and surgeons due to its increasing incidence, debilitating course and need for differentiated care. Our results encourage this relation and emphasize the role of the paediatric surgeon in the diagnose and early treatment of Chron’s perianal disease.
Perianal pediatric Chron's disease - an earlier call to the Pediatric Surgeon

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Objectives and Study: Crohn’s disease (CD) incidence is increasing worldwide, particularly in children and adolescents. Perianal Crohn’s disease (pCD) is a significant risk factor for a progressive and debilitating disease course. Data on the outcomes of children with pCD are scarce. Thus, we aimed to analyse the outcomes of this subset of patients in comparison with CD patients without perianal disease.

Methods: This study is a retrospective review of the clinical records of patients diagnosed with CD between April 2010 and April 2022. We analysed demographic variables, number of hospitalisations, perianal disease and its presentation, radiologic findings, laboratory data, medical treatments, and surgery interventions. Statistical analysis was performed with SPSS Statistics 28.0. Mann-Whitney or chi-square test were used, accordingly. p<0.05 was considered as statistically significant.

Results: Of the 68 CD patients included, 18 (26,5%) had perianal disease. Of those, 11 (66,1%) had complex perianal fistula, all characterized by pelvic magnetic resonance, 4 had perianal abscess, 2 had anal fissure and one had hemorrhoidal disease. Although pCD was more frequent in male, this difference was not significant (83,3 vs 62%). Median age at diagnosis was 13 years old, similar in both groups. We did not find differences in growth delay, haemoglobin, or calprotectin levels at diagnosis. However, pCD patients were more frequently hospitalised at the time of diagnosis, but with statistical ambiguity (66,7 vs 40%, p=0,05). Biologic treatment was more frequently used in pCD patients, without statistical significance (83,3 vs 64%, p=0,128). Unequivocally, pCD patients were more frequently submitted to surgery (33 vs 4%, p< 0,01). While one was submitted to ileocecectomy due to ileal disease, all other interventions focused on perianal disease – one had 4 surgeries due to his complex perianal fistula prior to diagnosis, 4 had perianal abscesses’ drainage (3, 4, 5 and 60 months after CD diagnose) and 2 patients had a seton placed.

Conclusions: In our series, we found a similar pCD prevalence to what is documented in the literature and higher predisposition to surgery. A special attention to these patients’ quality of life and future complications ought to be better acknowledged. The established worse clinical outcomes call for special focus in this subgroup of patients and close collaboration between paediatric gastroenterologists and surgeons.
P-041 (Poster of distinction)

Rare and severe complications in paediatric inflammatory bowel disease: a case-control study

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Objectives and Study: Paediatric inflammatory bowel disease (PIBD) patients (Crohn's disease (CD) and Ulcerative Colitis (UC)) are at risk of other severe and rare conditions. The aetiology of these complications remains unknown and there is a limited number of available studies investigating their incidence and causes. It remains unclear, if there is any relevance to the given treatment, the disease itself or if these complications occur randomly or related to some other factor. Moreover, the rare frequency of those complications negatively impacts the ability of specialists to manage them, and it makes statistical analysis rather challenging due to the small sample size and limited statistical power. Using data from a large international PIBD safety registry we have been able to detect rare complications that present a significantly higher incidence in the PIBD population compared to the general paediatric population. Using these data, we established a case control study to investigate possible aetiological factors for the complications of venous thromboembolic event (VTE) and renal failure.

Methods: Each involved centre reports the PIBD population covered annually, and the rare complications seen monthly, these data allow us to estimate the incidence of each complication. Two of the complications with the highest risk (VTE and renal failure) are then analysed to identify significant predictors using traditional frequentist approaches. This is a case-control study and logistic regression for 1:3 matched data for VTE and 1:4 matched data for renal failure were performed. The matching criteria were the duration of the disease, the disease classification (CD or UC) and the sex.

Results: The safety registry was started in October 2016 and is active to date. Overall, 222 paediatric gastroenterologists have participated in the safety registry in the five years of its operation. Currently, there are 127 international centres in 30 countries, which report to the registry covering a total of 62,460 patient-years. The total number of rare and severe complications that have been reported is 245. Two of the highest risk complications are the VTE, with incidence of 5.12 (95% CI 3.50-7.23) per 10,000 patients annually, which are comparable with our previously published data and renal failure cases with incidence of 4.16 (95% CI 2.56-5.76) per 10,000 patient-years. Logistic regression analysis suggests that increased disease activity and the use of corticosteroids and mesalazine are associated with both the appearance of VTE (Table 1) and renal failure events (Table 1). Despite the association of the use of corticosteroids with the increased disease activity, there is an additive effect of the use of corticosteroids in the appearance of those complications.

Table 1: Regression analysis for VTE

<table>
<thead>
<tr>
<th>Predictors for VTE</th>
<th>Odds ratio (VTE)</th>
<th>Lower 95% CI (VTE)</th>
<th>Upper 95% CI (VTE)</th>
</tr>
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<tbody>
<tr>
<td>Corticosteroids</td>
<td>15.627</td>
<td>2.657</td>
<td>91.925</td>
</tr>
<tr>
<td>Mesalazine</td>
<td>12.539</td>
<td>2.205</td>
<td>71.239</td>
</tr>
<tr>
<td>Disease activity</td>
<td>4.954</td>
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<td>22.741</td>
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</table>

<table>
<thead>
<tr>
<th>Predictors for renal failure</th>
<th>Odds ratio (renal failure)</th>
<th>Lower 95% CI (renal failure)</th>
<th>Upper 95% CI (renal failure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td>15.200</td>
<td>2.746</td>
<td>84.146</td>
</tr>
<tr>
<td>Mesalazine</td>
<td>30.213</td>
<td>4.182</td>
<td>218.292</td>
</tr>
<tr>
<td>Disease activity</td>
<td>32.150</td>
<td>5.893</td>
<td>179.357</td>
</tr>
</tbody>
</table>

Conclusions: PIBD patients are at a significantly higher risk for VTE, and renal failure complications as reported in our large international safety registry. In this case control study, we have identified potential risk factors to VTE and renal failure. The rarity of the presentation of these complications has major limitations. We aim to overcome the sample size limitations with the use of Bayesian statistics, which will allow us to validate our findings by combining these data with the opinion of experts.
Recommendations for Standardizing Magnetic Resonance Imaging-based Evaluation of Peri- 
nal Fistulizing Disease Activity in Pediatric Crohn’s Disease Clinical Trials

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sity Hospital, London Health Sciences Centre, Gastroenterology, London, Canada, 4Hospital for Sick
Children, Department of Diagnostic Imaging, Toronto, Canada

Objectives and Study: Perianal fistulae are common complications in children with Crohn’s disease 
(CD). A validated imaging assessment tool for quantification of disease activity is needed to evaluate 
treatment response. We aimed to identify magnetic resonance imaging (MRI)-based measures of dis-
ease activity and study design features appropriate for pediatric patients.

Methods: Seventy-nine statements relevant to MRI-based assessment of pediatric perianal fistulizing 
CD activity and clinical trial design were generated from literature review and expert opinion. State-
ment appropriateness was rated by a panel (N=15) of gastroenterologists, radiologists, and surgeons 
using modified RAND/University of California Los Angeles appropriateness methodology.

Results: The modified Van Assche Index and the Magnetic Resonance Novel Index for Fistula Imag-
ing in CD were considered appropriate instruments for use in pediatric perianal fistulizing disease clinical 
trials. Although there was concern regarding the use of contrast in pediatric patients, its use in clinical 
trials was considered appropriate. Appropriate trial inclusion criteria included a clinically evident 
fistula tract and radiological disease defined as at least one fistula or abscess on pelvic MRI. A co-pri-
mary clinical and radiologic endpoint and inclusion of a patient-reported outcome were also consid-
ered appropriate.

Conclusions: Outcomes of treatment of perianal fistulizing disease in children must include MRI, and 
existing multi-item measures can be adapted for children. Reliability and validity assessment specifi-
cally in pediatric patients is planned.

Conflict of Interest: EC has received an educational grant and speaker fees from AbbVie, Pfizer, and 
consulting fees from Alimentiv Inc. 
AMG has received consulting fees from Abbvie, Amgen, Bristol Myers Squibb, Lilly, Janssen, Merck, 
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VJ has received consulting/advisory board fees from AbbVie, Alimentiv Inc, Arena pharmaceuticals, 
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Model-Informed Precision Dosing with a Pharmacokinetic Dashboard is Now Available at the Bedside for Inflammatory Bowel Disease Patients Receiving Infliximab

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Objectives and Study: There is significant variability in infliximab (IFX) pharmacokinetics (PK) in children with multiple population PK models developed and several covariates identified to better predict drug clearance. Fortunately, therapeutic drug monitoring (TDM) is widely available and can be used to simplify model-informed precision dosing. However, empiric (“trial and error”) dose intensifications following TDM to achieve targeted levels can delay obtaining an optimal drug exposure and is a risk for supra-therapeutic levels. In this study, we highlight the formal processes to create a clinical decision support tool (CDST) for IFX and assess physician usability.

Methods: The development team included a PK software consultant, pharmacologists, paediatric gastroenterologists, nurses, software architects, and a human factor engineering firm (Pomiet, Dayton, OH, USA). CDST development occurred in 4 distinct phases (sprints). Design sprints started with structured interviews with key stakeholders, the creation of CDST wireframes (prototypes) and finished with an operational dashboard. Physician usability was assessed with the System Usability Scale (SUS).

Results: CDST design sprints included in-person interviews with 11 unique health care providers (8 physicians) over 26 sessions. During Phase I, clinicians noted current systems to dose optimize biologics are “cumbersome” and “not user-friendly” as key patient data to make informed decisions are in disparate locations within the electronic medical record (EMR). From Phase I to Phase IV, the design team used the wireframes for user feedback, made changes and developed the final CDST, RoadMAB™. Next, information services personnel integrated the CDST within the EMR. Patient data extraction occurs with a Fast Healthcare Interoperability Resources (FHIR) launch and produces an embedded browser within EMR. Additionally, our team created a standalone replica (web portal) of the EMR CDST that is secured by Microsoft Azure and hosted by Amazon Web Services. Our precision dosing CDST is supported by PK software that incorporates past IFX administrations and laboratory results (covariates and drug concentrations), conducts Bayesian PK estimation using the selected population PK model and displays the past and predicted concentration-time profiles (Figure 1a). The SUS was administered at three timepoints during the development to physicians’ with variable clinical experience. By the completion of RoadMAB™, the final mean (SD) SUS was 86.5/100 (15.2, Figure1b). Finally, in order to simplify precision dosing during IFX induction, we also created an induction (New Start) Wizard within RoadMAB™. Additional efforts will evaluate how model-informed dosing has impacted patient outcomes at our center.
Conclusions: The CDST for IFX is now integrated within the EMR and available as a web portal for bedside (point-of-care) precision dosing. Future clinical trials will test the feasibility and efficacy of RoadMAB™.
Objectives and Study: Efforts to standardize clinical trial design in inflammatory bowel disease (IBD) have included systematic reviews of endpoints in adults with Crohn’s disease (CD) and ulcerative colitis (UC). However, similar initiatives have not been performed in children (age < 18 years). We conducted a systematic review to summarize efficacy and safety endpoints that have been evaluated in pediatric IBD (pIBD) randomized controlled trials (RCTs).

Methods: We searched MEDLINE, EMBASE and CENTRAL from inception to October 14, 2020, for RCTs of pIBD patients treated with any drug or exclusive enteral nutrition. Efficacy and safety outcomes, definitions and measurement indices were extracted and stratified by decade of publication.

Results: Fifty-four RCTs (31 induction, 15 maintenance, 8 combined induction and maintenance; comprising 3,196 pediatric patients) were identified, with 1,504 children randomized to treatment and 1,530 to an active comparator/control. Clinical efficacy endpoints were reported in all trials, the most common being the Pediatric Crohn’s Disease Activity Index (PCDAI) and Pediatric Ulcerative Colitis Activity Index (PUCAI). There were 25 unique definitions (19 CD and 6 UC) for clinical response or remission. Only 14 trials incorporated endoscopic measurement. Biomarker outcomes were included in 57% (31/54) trials, with fecal calprotectin included as an outcome measure in 17% (9/54) of trials.

Safety outcomes were reported in 61% (33/54) of trials.

Conclusions: Considerable heterogeneity was identified in both outcome reporting and definitions of response and remission in RCTs of pIBD. These findings highlight the need for harmonization of outcome measures to improve design and conduct of pIBD RCTs.

Conflict of Interest: EC: educational grant/speaker fees from AbbVie, Pfizer and consulting fees from Alimentiv.
DT: consultation fees, research grants, royalties, or honorarium from Janssen, Pfizer, Hospital for Sick Children, Ferring, Abbvie, Takeda, Atlantic Health, Shire, Celgene, Lilly, Roche, ThermoFisher, and BMS.
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AMG: consulting fees from Abbvie, Amgen, Bristol Myers Squibb, Lilly, Janssen, Merck, Mylan, Pfizer; speaker fees Abbvie, Janssen, Nestle; investigator-initiated research support from Abbvie.
VJ: consulting fees from AbbVie, Alimentiv Inc, Arena pharmaceuticals, Bristol Myers Squibb, Celltrion, Eli Lilly, Ferring, Fresenius Kabi, GlaxoSmithKline, Genetech, Gilead, Janssen, Merck, Mylan, Pendopharm, Pfizer, Roche, Sandoz, Takeda, Topivert; speaker’s fees Abbvie, Ferring, Janssen Pfizer Shire, Takeda.
The Efficacy and Safety of Oral Vancomycin in the Treatment of Paediatric IBD: A Single Centre Retrospective Study

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Objectives and Study: The development of IBD is thought to involves a complex interplay of environmental, genetic and immune factors. Treatment is aimed primarily at suppressing the immune response, however luminal bacteria has been implicated in disease pathogenesis. The use of antibiotics in the treatment of IBD may be beneficial in modulating disease activity. Studies investigating the effectiveness of vancomycin in paediatric IBD (pIBD) remain limited. In this study we aimed to investigate the effect of vancomycin on disease activity in patients with pIBD.

Methods: Between January 2015 and April 2022 all children with a confirmed diagnosis of IBD, who received a course of oral vancomycin, were identified retrospectively using patient and prescribing records. Patients were excluded if treatment was primarily for the treatment of a toxin producing Clostridium difficile infection. Vancomycin treatment was prescribed per trust antimicrobial advice. Clinical activity was assessed by 4-point ‘Improve Care Now’ Physician Global Assessment (PGA) based on severity of symptoms (1=asymptomatic; 2=mild; 3=moderate; and 4=severe). Primary outcome was clinical response to PGA at completion of treatment, or for extended treatment regimens (≥3 months) the response was assessed at 3 months. Clinical remission was defined as a PGA of 1. Partial response was defined as PGA drop of ≥1 point. Secondary outcome was biochemical response with reduction in faecal calprotectin (FC), C reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Results: Ten patients (7 Female) were included in the study, with a median age at diagnosis of 4.4 years (range 6 months to 13 years.) Diagnoses were confirmed at endoscopy, included 2 Crohn’s disease, 1 Ulcerative colitis and 7 IBD-Unclassified (IBD-U). 30% of children at treatment initiation, were known to be colonised with non-toxin producing Clostridium difficile. One child received vancomycin as primary IBD treatment, 9 children were treated with vancomycin as adjuvant treatment. Additional IBD treatment included mesalazine (1), azathioprine (4), infliximab (2), Adalimumab (2), Ustekinumab (1), Vedolizumab (2) and Sirolimus (2). There was no significant change in the group average PGA score (median=3 at baseline and endpoint) from initiation to completion of treatment, or 3 months post-initiation for longer courses of vancomycin. Partial clinical response PGA score (of ≥1 point) was seen in 50% of children. Group averages for FC (median 1800 to 600 ug/g), CRP (median 18 to 5), and ESR (median 31 to 19 mm/h) numerically decreased from baseline to endpoint, but these differences were not statistically significant. No adverse or safety events were recorded.

Conclusions: Vancomycin treatment is associated with numerical reductions in several key inflammatory indices in paediatric IBD. The current study did not demonstrate significant change in group average Physician global assessment of disease activity. Larger prospective studies investigating vancomycin role as an adjuvant IBD therapy may be indicated.
Early proactive drug monitoring strategy of infliximab as monotherapy in pediatric inflammatory bowel disease is associated with good sustained clinical remission

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Objectives and Study: Monotherapy with Infliximab (IFX) could be as efficient as combination therapy with immunomodulators in the treatment and maintenance of remission in children with inflammatory bowel disease (IBD) if a proactive therapeutic drug monitoring strategy is adequately performed. This strategy may allow optimization of blood levels of IFX in order to obtain a sustained clinical remission.

Methods: A retrospective study was conducted amongst children with IBD, aged from 2 to 18 years old and diagnosed between June 2017 and June 2020. All patients were treated with IFX less than 30 days after diagnosis. Data concerning disease activity was collected at diagnosis and at one year after diagnosis. As per our protocol, IFX blood levels were collected before the third and/or fourth dose for all patients and regularly thereafter at the request of their physician. Adjustments in IFX infusion doses were made according to blood levels and clinical status. The primary outcome was clinical remission, defined by a PUCAI or a short PCDAI score < 10 without the need of corticosteroids, at one year after diagnosis. The secondary outcomes were the median (interquartile range (IQR)) dose of IFX (mg/kg) and the time intervals between IFX infusions at one year after diagnosis; the number of clinical relapses, the median (IQR) number of IFX dose changes and the median (IQR) number of blood trough levels of IFX done in the first year after diagnosis.

Results: A total of 103 patients were included (79% Crohn’s disease; median age at diagnosis is 13.2 years (IQR = 11.25-15.3)). At one year after diagnosis, 85 patients (83%) were in clinical remission. Thirty-four patients (33%) had at least one clinical relapse. In total, 63.1% of patients needed two or more IFX dose/interval optimization in the first year after diagnosis. The median initial IFX dose at induction was 8.4 mg/kg (IQR = 5.75-10). At one year, the median IFX dose per infusion was 8.93 mg/kg (IQR = 7.5-9.7) with infusions given 6 weeks apart or less in 79% of the patients. The median number of IFX trough levels per patient was 4 (IQR= 3.5-6.0) in the first year after diagnosis. At one year after diagnosis, 69% of patient were always on monotherapy with IFX alone and 11% were on combination therapy with IFX and an immunomodulator (azathioprine or methotrexate). IFX was discontinued in 17 patients due to antibodies occurrence (n=6), allergy (n=2), treatment failure (n=6), psoriasis (n=1), autoimmune hepatitis (n=1) or poor compliance (n=1).

Conclusions: Early treatment for IBD with IFX as monotherapy and a proactive optimization strategy is associated with a good sustained steroid free clinical remission. Most patients needed an increase of IFX dose during the first year of treatment. We therefore recommend to proactively monitor blood levels of IFX before the third and fourth dose of IFX and thereafter, in order to lower the risk of treatment failure and anti-infliximab antibodies occurrence.
Nutritional treatment with a specific exclusion diet plus a polymeric formula is comparable to standard nutritional therapy in newly diagnosed Crohn’s disease children.

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Objectives and Study: To compare the efficacy of a new nutritional therapy (Crohn’s disease exclusion diet (CDED) plus 50% of calories from a polymeric formula) versus the previously used standard nutritional therapy (EEN) in children with newly diagnosed Crohn’s disease (CD)

Methods: Retrospective, observational study. CDED group: every patient younger than 14 years of age, diagnosed with luminal (B1 phenotype) CD from June 1st 2019 to March 31st 2022 who received induction therapy with CDED plus 50% of calories from a polymeric formula (MODULEN IBD) for 6 weeks followed by CDED plus 25% calories from the same formula for another 6 weeks. EEN group: patients with CD treated with standard nutrition therapy (100% calories from MODULEN IBD for 6-8 weeks followed by free diet) treated from June 2015 up to May 31st 2019. Data were obtained from electronic records of each patient at baseline, 6, and 12 weeks. Data included weighted pediatric CD activity index (wPCDAI), fecal calprotectin (FC), albumin and CRP. Remission was defined as a wPCDAI < 12.5 points. Response was defined as a drop of 37.5 points in wPCDAI from baseline. Treatment failure was defined as the need to start steroid or biologic therapy in the first 6 weeks after the initiation of the nutrition therapy. Approval from local ethics committee was obtained (Reference 2021.280). Statistics: Independent samples Student’s T test, Fisher’s exact test.

Results: Twenty six patients were included in the study: 15 patients (5 girls) in the CDED group (ages from 6 to 13, mean 11.2 years) and 11 (5 girls) in the EEN group (mean age 10.9, from 7 to 13 years). No significant differences in age, gender or severity at baseline were observed. Both therapies were tolerated by 100% of the patients. Treatment failure was observed in 7 patients, 4 (36%) in the EEN group and 3 (20%) in the CDED group (p=0.41). At week 12, 37.5% of the patients in the EEN group were in steroid free remission compared to 62.5% patients in the CDED group (p=0.69). Regarding response, 80% of the patients in the CDED group responded and were steroid free compared to 63.6% in the EEN group (p=0.41). In those patients who completed 12 weeks of nutritional therapy without steroids or biologics FC showed a steady decrease in weeks 6 and 12 in the CDED group while in EEN patients a minor rebound in FC values was observed from weeks 6 to 12 (Table). On the other hand, median CRP values dropped in both groups in a similar fashion.

<table>
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<tr>
<th></th>
<th>baseline</th>
<th>Week 6</th>
<th>Week 12</th>
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<tbody>
<tr>
<td>EEN</td>
<td>FC (mcg/g)</td>
<td>501</td>
<td>1149</td>
</tr>
<tr>
<td>CDED</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEN</td>
<td>CRP (mg/dl)</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>CDED</td>
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Conclusions: Nutritional therapy with CDED plus 50% of calories from a polymeric formula shows similar efficacy to standard EEN in newly diagnosed luminal CD pediatric patients and might be used as first line therapy in this setting.

Conflict of Interest: J.J. Diaz has received speaker fees and travel grants from Nestle. S. Jimenez has received speaker fees and travel grants from Nestle.
Objectives and Study: This study describes the outcomes of an enhanced recovery after surgery (ERAS) protocol in a cohort of pediatric patients undergoing abdominal surgery for inflammatory bowel disease (IBD) and compares the main outcomes with those of a traditional non-ERAS group of patients.

Methods: The hospital medical records of pediatric patients (aged 0–18 years) who underwent abdominal surgery for IBD at two academic referral centers from January 2016 to June 2021 were reviewed retrospectively. The ERAS protocol included preoperative education and counseling, antibiotic prophylaxis, minimally invasive surgical approach whenever possible, multimodal analgesia, postoperative nausea and vomiting prophylaxis, early enteral feeding, early removal of wound drainage and urinary catheters, and early mobilization. Preoperative, intraoperative, and postoperative data were collected for each procedure. The primary outcomes were timing of first defecation, postoperative complications, and length of hospital stay (LOS). The differences in each outcome between the ERAS group and the non-ERAS group were investigated.

Results: Thirty-three children who had 61 abdominal surgeries for IBD were included. The median age at surgery was 13.6 (4.6-17.8). Surgery was performed for ulcerative colitis (UC) (n = 28, 45.9%), Crohn’s disease (CD) (n = 28, 45.9%), or IBD unclassified (IBDU) (n = 5, 8.2%). The non-ERAS group included forty surgical procedures (65.5%), while the ERAS group included 21 (34.5%). Postoperative complications occurred in 28 (45.9%) cases. They were surgical (i.e., intestinal obstruction, anastomotic dehiscence) in 33 (54.1%) cases and medical (i.e., fever, vomiting, wound infection) in the remaining ones. The postoperative complication rate was significantly lower in the ERAS group than in the non-ERAS group (29.6% vs. 55%, p = 0.049) (Figure 1).
The type of complication (medical vs. surgical) did not differ between the two groups (p = 0.557). The first defecation occurred earlier in the ERAS group than in the non-ERAS group (p < 0.001). In the ERAS group, all surgical procedures were followed by the first defecation ≤ 24 hours after surgery, whereas in the control group, the first defecation occurred ≤ 24 hours after surgery in 17 cases (42.5%), between 24 and 72 hours in 13 cases (32.5%), and > 72 hours in the remaining cases. The overall median LOS was 6 days ± 7.52, with no difference between the two groups (5 days ± 6.92 in the ERAS group and 8 days ± 7.80 in the non-ERAS group, p = 0.114).

Conclusions: The implementation of ERAS in pediatric IBD surgery resulted in better outcomes than traditional perioperative care, especially in terms of postoperative complication rate and bowel function recovery. More pediatric studies are needed to validate these findings and support the application of ERAS in children.
Adalimumab use in paediatric inflammatory bowel disease: A single centre real-life experience

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Objectives and Study: Anti-TNF-α, including infliximab and adalimumab (ADA), plays a crucial role in the treatment of paediatric inflammatory bowel disease (PIBD). This study evaluates the efficacy of ADA in children ≤ 19 years in a single European centre.

Methods: A 6-year retrospective analysis of prospectively collected data of PIBD patients treated with ADA (10/2015 onward). Wellbeing, clinical and laboratory findings were assessed at each visit. A mean, median and a standard deviation were calculated where applicable. ANOVA (analysis of variances) was used for evaluation of presence of statistically significant differences and a $P$-value ≤ 0.05 was regarded as such.

Results: ADA, all originator, was used in 31 patients. All of them were diagnosed with Crohn’s disease (CD). The mean age at diagnosis was 14.6±2.8 years (range 6.6-18.2 years). The mean interval from diagnosis till commencement of ADA was 6.9 months (0.25-36 months). Step-up was used 17x and top-down 15x. A top-down approach was indicated in patients with extraintestinal manifestations, fistulizing disease, severe growth impairment and affections of the proximal gastrointestinal tract. Adjacent treatments at the time of commencement of ADA were azathioprine (18/31), CD exclusion diet (7/31), exclusive enteral nutrition (6/31), steroids (4/31), methotrexate and 5-aminosalicylates (both 3/31).

Mean CRP at the time of ADA commencement was 8.8 mg/l (1.0-44.4 mg/l), ESR 21 mm/hour (1-66 mm/hour), leukocytes 8.3x10⁹/l (3.3-22.0x10⁹/l), haemoglobin 118.3 g/l (68-150 g/l), platelets 422x10⁹/l (232-828 x10⁹/l) and faecal calprotectin (FC) 901.1 μg/g (95.2-5041.9 μg/g). At the end of induction period, CRP, ESR and FC showed a significant decrease ($P$< 0.01). Blood count parameters failed to show that ($P$>0.05). Mean ADA trough levels at the end of induction period were 18.4±2.3 μg/ml. For maintenance of trough levels (≥7.5 μg/ml), weekly administration was required in 5 cases. During the follow-up period, surgical intervention was required 2x (ileocecal resection 1x and stricturoplasty 1x). Adverse side effects consisted of a skin reaction 1x and reversible hair loss 1x. Due to loss of response, 3 patients had to be switched out-of-class to ustekinumab. The mean time to loss of response since ADA commencement was 23.3 months (16-30 months). Antibody formation after 23 months of treatment led to switching one patient to infliximab. One patient was lost to follow-up.

Conclusions: These data show that ADA is effective in achieving laboratory and clinical remission in PIBD patients. Maintenance of trough levels may sometimes require weekly administration of ADA. Loss of response may occur. Adverse reactions were minimal.
**P-050**

**Crohn's disease exclusion diet: A single centre real-life experience.**

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**Objectives and Study:** According to ECCO-ESPGHAN (European Crohn's and Colitis Organization, European Society for Paediatric Gastroenterology, Hepatology and Nutrition) consensus guidelines, exclusive enteral nutrition (EEN) is the first line therapy for induction of remission in children with active luminal Crohn's disease (CD). Steroids may be considered in cases when EEN is not an option. However, adherence to EEN is not ideal and, according to various sources, ranges from 50-91 %. This poor adherence is mainly due to palatability and monotony of EEN. Many attempts have been made to find an alternative to EEN. One of them is Crohn's disease exclusion diet (CDED) with partial enteral nutrition (PEN), which, based on published data, shows promising results in not only efficacy and safety, but also adherence. This study evaluates the efficacy of CDED with PEN in a single European centre.

**Methods:** Retrospective evaluation of prospectively collected dated of children treated with CDED with PEN from 10/2019 until 4/2022. Wellbeing, anthropometric data, and laboratory results were evaluated prior to the commencement of CDED with PEN and at the end of both phases 1 and 2. A mean, median and a standard deviation were calculated were applicable. ANOVA (analysis of variances) was used for evaluation of presence of statistically significant differences and a $P$-value ≤ 0.05 was regarded as such.

**Results:** CDED with PEN was used in 19 patients. The mean age at diagnosis was 14.8±3.9 years (range 3.0-17.1 years). At the time of evaluation, 17/19 patients have completed the first phase and 15/19 have completed the second. At the same time, 2 patients were still in phase one and 1 was in phase two. One patient decided to quit CDED with PEN at the end of the first phase and another at the end of the second. The completion rate of phase one is 94 % and of the second 93,75 %. At the time of commencement of CDED with PEN, dietary intervention was the only treatment in 10/19 patients. Three patients were using Azathioprine (AZA), 2 5-aminosalicylic acid (5-ASA), 1 Methotrexate (MTX) and another Prednisone. At the end of phase one, 8 patients were on anti-TNF-α, the same number was using AZA, 2 5-ASA and 1 MTX. At the end of the second phase, anti-TNF-α was used in 12 patients, AZA in 8, MTX in 3 and both anti-IL12/23 and 5-ASA in 1 patient. At the end of both phases, CRP, ESR (erythrocyte sedimentation rates) and faecal calprotectin have shown a statistically significant decrease ($P≤ 0.01$). While platelet counts did not show a statistically significant decrease at the end of the first phase ($P > 0.05$), it did show so at the end of the second ($P≤ 0.01$). Other followed parameters failed to show a significant difference at the end of the follow-up period.

**Conclusions:** These data support that CDED with PEN is well tolerated by children with a very high adherence rate. They also confirm that inflammatory markers, including faecal calprotectin, decrease statistically significantly at the end of both phases. CDED with PEN should be considered as an alternative to EEN and steroids in induction of remission of luminal CD in children.
Anti-TNF-α in paediatric inflammatory bowel disease: A single centre real-life experience

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Objectives and Study: Anti-TNF-α (ATA) plays a crucial role in the treatment of paediatric inflammatory bowel disease (PIBD). This study evaluates the efficacy of ATA in children ≤ 19 years in a single European centre.

Methods: A 6-year retrospective analysis of prospectively collected data of PIBD patients treated with ATA (10/2015 onward). Wellbeing, clinical and laboratory findings were assessed at each visit. A mean, median and a standard deviation were calculated where applicable. ANOVA (analysis of variances) was used for evaluation of presence of statistically significant differences and a $P$-value ≤ 0.05 was regarded as such.

Results: ATA was used in 52 patients. The mean age at diagnosis was 12.4±3.5 years (range 2.7-18.2 years). Crohn’s disease (CD) was diagnosed 44x, ulcerative colitis 5x, IBD-undifferentiated 1x and very early onset IBD 2x. The mean interval from diagnosis till commencement of ATA was 9.2 months (0-46 months). Step-up was used 29x and top-down 23x. Top-down was indicated in patients with extraintestinal manifestations, fistulizing disease, severe growth impairment and affections of the proximal gastrointestinal tract. Infliximab (IFX) was used in 21 patients and adalimumab (ADA) in 32. ADA was only used in CD. Due to formation of antibodies, a switch within class from ADA to IFX was required twice. Anaphylaxis led once to a switch from IFX to ADA. Loss of response led to switching 3 patients out-of-class from ADA to ustekinumab. Adjacent treatments at the time of ATA commencement were azathioprine (37/52), steroids (12/52), 5-aminosalicylates (7/52), CD exclusion diet (8/52), exclusive enteral nutrition (7/52) and methotrexate (3/21). Mean CRP at the time of commencement of ATA was 9.3 mg/l (1.0-28.1 mg/l), ESR 24 mm/hour (1-115 mm/hour), leukocytes 8.9x10^9/l (3.3-22.0x10^9/l), haemoglobin 117.7 g/l (68-150 g/l), platelets 437x10^9/l (218-828 x10^9/l) and faecal calprotectin (FC) 921.8 μg/g (93.0-5041.9 μg/g). At the end of induction period, CRP, ESR and FC showed a significant decrease ($P$< 0.01). Blood count parameters failed to show that ($P$>0.05). Mean IFX trough levels at the end of the induction period were 12.6±5.6 μg/ml. The mean interval between maintenance doses for reaching desired trough levels (≥5.0 μg/ml) was 7±1.4 weeks. Mean ADA levels at the end of induction were 18.4±2.3 μg/ml. For maintenance of trough levels (≥7.5 μg/ml), weekly administration was required in 5 cases. During the follow-up period, surgical intervention was required 3x. Adverse side effects consisted of skin reactions 2x, reversible hair loss 1x and anaphylaxis 1x. One patient was lost to follow-up.

Conclusions: These data support that ATA is highly effective in reaching remission in PIBD. Some children require intensified maintenance regimen for IFX and ADA. The number of recorded adverse side effects is minimal.
Indirect and out-of-pocket disease-associated costs in paediatric inflammatory bowel disease: a nation-wide cross-sectional analysis from the Canadian Paediatric IBD Network

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Objectives and Study: Data on paediatric inflammatory bowel disease (IBD)-associated indirect and out of pocket costs are limited. We aimed to estimate indirect (lost work hours and productivity) and out of pocket (OOP) paediatric IBD-associated costs in Canada.

Methods: In a nation-wide cross-sectional analysis, caregivers of children with IBD were invited to complete a questionnaire on lost work hours and OOP costs related to IBD in the 4 weeks prior to the survey. Participants were re-invited to periodically answer the same questionnaire every 3-9 months for 2 years. Lost productivity was calculated using the Human Capital method. Costs were reported in 2018 inflation-adjusted Canadian dollars. Predictors of high cost users (top 25%) were examined using binary logistic regression.

Results: Consecutive 243 (82 incident cases) of 262 (92.7%) approached participants completed the first survey with a total of 450 surveys longitudinally completed over 2 years. The median annual indirect cost per patient was $5,966 (IQR $1,809- $12,676), with $5,721 (IQR $1,366-$11,545) for Crohn's disease (CD) and $7,007 (IQR $2,428-$14,057) for ulcerative colitis (UC) (p=0.11). The annual median per patient OOP costs were $4,550 with $4550 for CD and $5038 for UC (p=0.53). Longer travel distance to clinics was associated with higher OOP costs [odds ratio= 4.16 (95% confidence interval, 1.01-17.21)].

Conclusions: Indirect and OOP IBD-associated costs are substantial and more likely to affect families living in remote communities. The effect of interventions such as virtual platforms, telephone and outreach clinics should be explored.
New EUROKIDS registry for diagnosis of paediatric IBD

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Objectives and Study: The original EUROKIDS registry is a European prospective web-based cohort study of newly diagnosed PIBD patients. Initiated by the Paediatric IBD Porto group of ESPGHAN, it launched in 2004 and based off the initial Porto criteria, operating with the traditional classifications of IBD into 3 subtypes: Crohn’s Disease (CD), Ulcerative Colitis (UC), and IBDU-Unclassified (IBDU). Once the revised Porto PIBD-Classes criteria and diagnostic algorithm were published in 2017 which described clearer subtypes: small ± large bowel CD, isolated colonic CD, UC, atypical UC, and IBDU, we updated EUROKIDS incorporating the PIBD-Classes criteria and diagnostic algorithm. Objectives are 1. to validate the diagnostic PIBD classes in the registry, 2. to accurately phenotype this cohort and compare to the EUROKIDS cohort of 2004-2009. 3. to assess completeness and quality of diagnostic work-up, compared to the EUROKIDS cohort of 2004-2009. The revised PIBD-Classes and algorithm have already been validated as accurate constructs to standardise the 5 subtypes of PIBD. Now their implementation into the EUROKIDS registry needs to be evaluated to ensure their accuracy is maintained. We appraised the PIBD-Classes criteria and diagnostic algorithm’s incorporation into the updated EUROKIDS website by assessing the level of concordance between EUROKIDS’ algorithm-generated diagnoses and physicians’ clinically-generated diagnoses.

Methods: Anonymised data at diagnosis (single timepoint) concerning endoscopy information, histology, radiology, disease behaviour, and Paris Classification is entered within 3 months of a patient’s diagnosis. From this data, the EUROKIDS system automatically scores whether the 23-features of the PIBD-Classes criteria are present/absent, resulting in a point total per class which the algorithm translates into a diagnosis. This diagnosis can be agreed with or contested by the physician. The presence or absence of the 23-items of the PIBD-Classes criteria, and the subsequently related diagnostic algorithm’s diagnoses, were accessed from the EUROKIDS database as well as the physicians’ clinically assigned diagnoses per patient. This data was then analysed for concordance, sensitivity, and specificity. Because of a systematic website error website, manual corrections had to be made to the point totals of 12 patients. We present the data of patients that were registered in the first 3 months of the registry (Jan-March 2022).

Results: 96 children (4-18 years old) were included by the 11 centres actively participating across 8 countries. Overall concordance was high (85%, 82/96) with 14 disagreements between the physicians’ and algorithm’s diagnoses. Potential causes for disagreement are framing bias, incomplete diagnostic work-up, or true non-concordance. Sensitivity and specificity values per phenotype were very high with a range from 73.7% - 100% and 92.5% – 100%, respectively.
Conclusions: We showed the validity of the PIBD-Classes criteria with the algorithm’s implementation into EUROKIDS with good accuracy in diagnosing the 5 subtypes of PIBD. After correction of the website-based errors, EUROKIDS continues to successfully collect and standardise patient data. The implementation of the PIBD-Classes criteria and algorithm is helpful in clinical practice and contributes to an accurately phenotyped cohort of PIBD patients.
P-054 (Poster of distinction)

The Lémann Index has insufficient validity in children: a report from the prospective multicenter ImageKids study


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Objectives and Study: Assessment of structural bowel damage in pediatric Crohn’s disease (CD) is possibly different than in adults given the shorter disease duration in a typical pediatric cohort and the more extensive disease. The Lémann Index (LI) and its recent updated revision (RLI) is a tool for measuring bowel damage in CD, developed in adults. We aimed to explore the validity, reliability and responsiveness of the RLI in pediatric CD in the prospective multicenter ImageKids study.

Methods: This is a planned major analysis of the prospective ImageKids study in which children with CD underwent magnetic resonance enterography (MRE), pelvic MRI (pMRI) and endoscopy concurrently, half of whom were followed for 18 months when MRE was repeated. MREs and pMRIs were centrally read. Reliability, as well as construct and discriminative validity were assessed on the baseline visit while responsiveness and test-retest reliability were explored on the longitudinal cohort.

Results: We included 240 children (mean age 14.2±2.5 years, median disease duration 2.2 years (IQR 0.25-4.42)), median baseline RLI 4.14 (IQR 0.9-8.4)). The RLI had an excellent inter-observer reliability (ICC=0.94, 95%CI 0.92-0.95). The RLI had poor, although statistically significant, correlation with radiologist and gastroenterologists global assessments of damage and with serum proteomic levels of fibrotic markers (r=0.15-0.32, most p<0.05). The RLI had low discriminative validity to detect damage (AUROC, 0.69 [95%CI 0.62-0.75]; figure). There was low responsiveness at 116 repeated MREs to differentiate improved from unchanged children (AUROC 0.57 [95%CI, 0.45-0.70]). Test-retest reliability among stable patients was high (ICC=0.86, 95%CI 0.76-0.92).

Conclusions: Overall, the RLI had insufficient psychometric performance for recommending its use in children. An age-specific sensitive index may be developed for children who have shorter disease duration than in typical adult cohorts.
**Conflict of Interest:**

**GF:** received last 3 years consultation fee from Abbvie and Lilly  
**MLG:** received in the past 3 years AbbVie investigator-initiated research grant and honoraria, Samsung honoraria  
**PC:** received during the past 3 years speaker fees, consultant fees or grants from Abbvie, Amgen, Janssen, and Takeda.  
**AMG:** received during the past 3 years consultant fees from Abbvie, Amgen, Bristol Myers Squibb, Lilly, Janssen, Merck, Pfizer; speaker fees from Abbvie, Janssen, Nestlé; investigator-initiated research grant from Abbvie.  
**DT:** received last 3 years consultation fee, research grant, royalties, or honorarium from Janssen, Pfizer, Hospital for Sick Children, Ferring, Abbvie, Takeda, Atlantic Health, Shire, Celgene, Lilly, Roche, ThermoFisher, BMS.
Prevalence and incidence of fistulising Crohn’s disease and associated treatment patterns in paediatric patients in the United States

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Objectives and Study: There are limited epidemiologic data on paediatric patients with fistulising Crohn’s disease (CD) and associated treatment patterns. Although some biologics have proven to be effective in delaying disease progression in some patients, surgical intervention is often required. The aim of this study was to estimate the incidence rate and prevalence of fistulising CD in paediatric patients in the US, and describe treatment patterns among incident cases.

Methods: This retrospective cohort study was conducted using Optum claims data from 2017–2019. Patients aged 6 to 17 years, with ≥365 days of continuous enrolment and initial (index) diagnosis of fistula and CD were identified during the study period. Incident cases of fistulising CD were defined as patients without claims for any fistulising CD International Classification of Diseases 10th revision (ICD-10) diagnosis codes prior to the index diagnosis. Prevalent cases were defined as patients with claims with fistulising CD ICD-10 diagnosis codes prior to the index diagnosis. Crude age- and sex-adjusted incidence rates and prevalence were estimated. Among incident cases continuously enrolled for ≥1 year after the index diagnosis, treatments received after the index CD fistula diagnosis were examined and reported on a quarterly and annual basis.

Results: Among 2,173,445 paediatric patients at risk during the study period, (mean age 12 years [standard deviation 3], 49% female), a total of 158 incident and 249 prevalent cases of fistulising CD were identified. The crude incidence rates and prevalence for 2017–2019 were 4.32 per 100,000 person-years (95% confidence interval [CI] 3.70–5.05) and 11.46 per 100,000 persons (95% CI 10.12–12.97), respectively, with minimal change after adjusting for age and sex. Only 13 (aged 6–11 years) and 68 (aged 12–17 years) incident cases fulfilled the criterion of being enrolled for ≥1-year post-index diagnosis and were included in treatment pattern analysis. Overall, >75% of patients were prescribed anti-tumour necrosis factor (TNF) therapies within 1 year of receiving an incident fistulising CD diagnosis; most frequently infliximab (59.26%) or adalimumab (28.40%). Antibiotic and corticosteroid use in Quarter 1 was more common in patients aged 12–17 years than in patients aged 6–11 years (Table); the difference in cumulative use of these therapies was also greater by Quarter 4. For patients aged 6–11 years, 23% underwent surgery (mainly seton placement); none received total parenteral nutrition (TPN) within 1-year post-index diagnosis. For patients aged 12–17 years, 34% underwent surgery (mainly colon resection) and 15% received TPN within 1-year post-index diagnosis.

Table. Treatment patterns in patients with incident fistulising Crohn’s disease (cumulative)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Patients who received medication of interest, n (%)</th>
<th>3 months post-index diagnosis (Q1)</th>
<th>6 months post-index diagnosis (Q2)</th>
<th>9 months post-index diagnosis (Q3)</th>
<th>12 months post-index diagnosis (Q4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6–11 years</td>
<td>Antibiotics</td>
<td>3 (23.08)</td>
<td>3 (23.08)</td>
<td>3 (23.08)</td>
<td>4 (30.77)</td>
</tr>
<tr>
<td>(n=13)</td>
<td>Corticosteroids</td>
<td>5 (38.16)</td>
<td>5 (38.16)</td>
<td>7 (53.85)</td>
<td>7 (53.85)</td>
</tr>
<tr>
<td></td>
<td>Immunomodulators</td>
<td>2 (15.38)</td>
<td>2 (15.38)</td>
<td>4 (30.77)</td>
<td>4 (30.77)</td>
</tr>
<tr>
<td></td>
<td>Anti-TNF agents</td>
<td>7 (53.85)</td>
<td>8 (61.54)</td>
<td>8 (61.54)</td>
<td>10 (76.92)</td>
</tr>
<tr>
<td>12–17 years</td>
<td>Antibiotics</td>
<td>26 (38.24)</td>
<td>27 (39.71)</td>
<td>33 (48.53)</td>
<td>35 (51.47)</td>
</tr>
<tr>
<td>(n=68)</td>
<td>Corticosteroids</td>
<td>30 (44.12)</td>
<td>34 (50.00)</td>
<td>40 (58.82)</td>
<td>43 (63.24)</td>
</tr>
<tr>
<td></td>
<td>Immunomodulators</td>
<td>11 (16.18)</td>
<td>17 (25.00)</td>
<td>19 (27.94)</td>
<td>22 (32.35)</td>
</tr>
<tr>
<td></td>
<td>Anti-TNF agents</td>
<td>53 (77.94)</td>
<td>54 (79.41)</td>
<td>55 (80.88)</td>
<td>55 (80.88)</td>
</tr>
</tbody>
</table>

Q, quarter; TNF, tumour necrosis factor.
Conclusions: The prevalence and incidence rates of fistulising CD are low among paediatric patients in the US and below the rates observed in adult patients. Paediatric patients with fistulising CD are commonly treated with biologics, particularly anti-TNF agents, with a considerable proportion receiving surgical intervention.

Conflict of Interest: YF, LZ, SF are employees of Boehringer Ingelheim. GYM is a consultant for Abbvie, Arena, Boehringer Ingelheim, Bristol Meyers Squibb, Ferring, Janssen, Nephroceuticals, Oshi, Pfizer, Samsung Bioepis, Shield, Takeda, Techlab, and receives research support from Pfizer. WAF declares having attended advisory boards and/or received consultancy fees from AbbVie, Apple Tree Life Sciences, Apertor, Boehringer Ingelheim, Eli Lilly, and Janssen.
A prospective cross-sectional mixed-methods study evaluating dietary modifications in children with Inflammatory Bowel Disease.

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Objectives and Study: Food avoidance (FA) is commonly seen in patients with Crohn’s disease (CD) compared to Ulcerative Colitis (UC) and to a greater extent in those with symptoms. Recent studies have reported success in controlling symptoms and inflammation using elimination diets in patients with IBD, leading to a resurgence of patients interest in dietary manipulation. We aimed to determine the frequency of dietary manipulation, sources of dietary advice, dietary modification patterns in children with IBD.

Methods: Using a mixed-methods study, a validated dietary beliefs and practices questionnaire was used to collect qualitative data in children with IBD attending Perth Children’s Hospital. Quantitative assessment of clinical activity (PCDAI/PUCAI) recorded on the day of appointment was matched with simultaneously collected qualitative data. Disease activity was classified; as inactive (PCDAI/PUCAI <10), mild (PCDAI or PUCAI<30) and moderate (PCDAI or PUCAI >30). The main outcomes of interest were a) prevalence of dietary modifications in symptomatic vs. asymptomatic patients c) the source of information for the parent/patients modifying their diet d) an overall satisfaction in receiving dietary advice from different sources.

Results: 64 Children (34 Males, mean age 13.3 years) with IBD (28 CD, 36 UC) participated in the survey between April and December 2021. Survey was filled out jointly by patients and parent (n=38) followed by patients (n=19) and parents alone (n=7). Therapies of patients included for analysis were biologics (35/64, 55%) followed by oral Immunomodulators (16/64, 25%) and oral ASA or steroids 13/64 (20%). Disease activity at inclusion was inactive (29/64, 45%), mild (31/40, 48%), and moderate in 4/64, 7%. The distribution of active disease was similar among IBD subtype’s (UC vs. CD) or sex (female 19/31 vs. male 16/34, p=0.3). Almost two-thirds (42/64, 65%) attributed symptoms with certain foods. Abdominal pain and cramps (35/64, 55%) were most commonly reported symptoms, followed by diarrhea (31/64, 36%), nausea and bloating (22/64, 34%). Females attributed symptoms with foods more than males (24/30 (80%) vs. 18/34 (53%), p=0.03). Food avoidance (FA) was reported by 50% (31/64), FA was frequent in females vs. males (19/30 (63%) vs 12/34 (35%), p=0.04). The most frequently excluded foods in symptomatic patients were milk products (9/31, 29%), confectionary/sugary foods (9/31, 29%). Fruits/vegetables, white meat, supplementary nutrition and soups were frequently consumed to improve symptoms (Figure 1). FA was common when disease is active vs. inactive (19/31 vs. 9/33, p=0.02). The main source of dietary advice was through gastroenterologists and/or dietitian (n=26/64, 40%), almost one-thirds excluded their diet based on non-expert advice. Females were more interested in receiving a formal diet advice to control IBD (Mean value on visual analog scale (VAS) 81.1 vs. 68.2, p=0.06). A higher satisfaction was reported when receiving diet advice from Gastroenterologist and or Dietitian, compared to family members (Mean VAS 76 vs. 67.9, p=0.03) or a family physician (76 vs. 59.25, p=0.001).
Conclusions: More than 50% modify their diet post diagnosis, more when symptomatic. Females frequently avoid foods to control symptoms compared to males (63% vs. 35%). The most commonly avoided foods were dairy, confectionery, grains and red meat.
**Prevalence of Growth Restriction in a Contemporary Paediatric Inflammatory Bowel Disease Cohort**

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**Objectives and Study:** Growth Restriction is one of the most common complications of Inflammatory Bowel Disease (IBD) in paediatric patients. Growth Restriction was reported in 15-40% of Crohn’s disease and 3-10% of Ulcerative Colitis patients. This audit aims to evaluate the relationship between Inflammatory Bowel Disease and growth restriction with respect to the IBD subdivisions: Crohn’s Disease (CD), Ulcerative Colitis (UC), IBD-Unknown (IBD-U) and Very Early Onset IBD (VEO-IBD) patients at diagnosis and present. It will also discuss the association between severity of growth restriction and terminal ileum (Ti) involvement.

**Methods:** This project encompasses a cohort of 150 paediatric patients evaluated over a ten-year period. The data set was derived from patients currently under the care of the Paediatric Gastroenterology service at St George’s University Hospital from 2011 to 2021. Information was gathered from patient documents and recorded with respect to IBD classification. Height and weight were recorded at diagnosis and present (June 2021) and Z scores were calculated. The scores were then classified into categories of growth restriction severity. For this audit, growth restriction was defined as a Z score of less than or equal to -2 (2 or more SD below the mean).

**Results:** After excluding patients that had not been monitored in the last year, there were 100 patients left in the study. Results were analysed at diagnosis and present to review data trends.

At diagnosis, nine patients fell under the growth restriction classification. Of these patients: 67% had CD, 22% had UC and 11% had IBD-U. In the CD group, 83% had moderate and 17% had severe restriction. Of the CD patients falling into the moderate category, 66.7% had 10-19cm of Ti involvement and 33% had >20cm of involvement. Precise length of Ti involvement was not documented in the severe category. All patients with UC and IBD-U had moderate restriction and unknown Ti involvement.

At present, eight patients fell under the growth restriction classification. Of these patients: 75% had CD, 12.5% had UC and 12.5% had IBD-U. In the CD group, 83% had moderate and 17% had severe restriction. Of the CD patients falling into the moderate category, 50% had 10-19cm of Ti involvement, 25% had >20cm and 25% had no Ti involvement. Once again, all patients with UC and IBD-U had moderate restriction and unknown Ti involvement.
**Conclusions:** This audit demonstrated that growth restriction occurs in CD, UC and IBD-U, but primarily affects Crohn’s disease. In all the IBD subcategories, moderate growth restriction is the most common, however only the Crohn’s cohort exhibits severe growth restriction. When comparing growth restriction at diagnosis and at present, there is not a great deal of change in the prevalence. This indicates that when growth restriction is seen, it is usually present at diagnosis rather than developing over time. Terminal ileum involvement was more difficult to predict as there was insufficient evidence to make a correlation, likely because growth restriction is multifactorial. Due to the COVID-19 pandemic, there has been a lack of monitoring of IBD patients. As the NHS returns to full function, improvements can be made to ensure regular height, weight and radiology monitoring. Future investigations should involve a larger cohort to further investigate these findings.
Sustainability in paediatric patients with Crohn’s disease – analysis from Czech national registry of biologic treatment (CREdIT)

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Objectives and Study: Comparative studies, even head-to-head trials, comparing different biologic agents in paediatric patients with Crohn’s disease (CD) are missing. Recent study suggested that adalimumab treatment was superior to other agents in sustainability of the drug. We aim to assess association of sustainability and different biologic drugs.

Methods: Using Czech national prospective registry of biologic and modern therapy of IBD (CREdIT) we identified 467 courses of biologic treatment in paediatric CD patients. Using mixed effects cox models we attempted to identify an association between a biologic agent and sustainability of the treatment. A patient and a biologic centre were added as random effect into the models.

Results: Among included 445 observations (176 female, 40%), 200 were with adalimumab (45%), 201 with infliximab (45%), 32 with ustekinumab (7%) and 12 with vedolizumab (3%). Most of the observations were from the first line of the biologic treatment (first: 331, 74%, second 83, 19%, third 27, 6%, fourth and fifth 4, 1%) and with concomitant immunosuppressive therapy at beginning of the treatment course (351, 79%).

Comparing to adalimumab treatment, sustainability of infliximab was lower (hazard ratio [HR] 0.55, 95% CI 0.32-0.94) in mixed effect cox model adjusted for the line of the treatment, age, C-reactive protein level and immunomodulatory therapy at the time of treatment initiation and for centre and individual in random part of the model. We did not find different sustainability of vedolizumab and ustekinumab however, limited number of these observations were included in the analysis.
Conclusions: In paediatric CD patients, sustainability of biologics seems to be consistently slightly higher with adalimumab compared to infliximab.
Pediatric Patient and Caregiver Satisfaction with the use of Transabdominal Bowel Ultrasound in the Assessment of Inflammatory Bowel Disease

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Objectives and Study: Transabdominal bowel ultrasound (TABUS) is emerging as an attractive, non-invasive tool in inflammatory bowel disease (IBD). Patient and caregiver experience with TABUS is not well described. We aimed to determine pediatric patient and caregiver satisfaction with TABUS and the impact of IBD severity, gender, age, and a history of anxiety on satisfaction.

Methods: Pediatric patients (0-18 years old) with suspected IBD prospectively underwent baseline TABUS, magnetic resonance enterography (MRE), blood work, stool studies, and endoscopy. Patients and their caregiver each completed a cross-sectional satisfaction questionnaire (5-point Likert scale) after the baseline investigations.

Results: There were 54 patients included (67% male). The majority were completely satisfied and strongly agreed that TABUS was better tolerated than other investigations (Figure 1), regardless of disease severity (p>0.05). Patients with higher Simple Endoscopic Score for Crohn Disease (SES-CD) scores felt that TABUS increased their understanding of their IBD (p<0.05) and disease location (p<0.05). Patients with crohn’s disease had similar responses to those with ulcerative colitis, but more strongly agreed that TABUS was better than MRE and endoscopy (p<0.05). In contrast to the patients, caregivers of patients with more severe IBD disagreed that TABUS was tolerated better than MRE (p<0.01), endoscopy (p<0.05), and IV insertion (p<0.05). Those with anxiety did not have an increased level of worry about potential ultrasound findings (p>0.05). There were no differences between genders (p>0.05). Teenagers (>12 years) were more satisfied with the information they received about the procedural steps, compared to younger patients.
Conclusions: Pediatric patients and their caregivers were highly satisfied with TABUS, preferring it to other modalities. It did not lead to increased worry, and was particularly important in those with severe IBD, which is underestimated by their caregiver. These findings support wider implementation of this well tolerated and preferred monitoring tool in pediatrics.
P-060

Treatments received within 6 months after diagnosis of Pediatric Crohn’s Disease: Analysis of the Japanese Pediatric Inflammatory Bowel Disease Registry.


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Objectives and Study: The Japan Pediatric Inflammatory Bowel Disease (IBD) Registry includes newly diagnosed IBD patients aged under 17 years from 23 hospitals with pediatric IBD specialists. Follow-up data were recorded every 6 months. The registry began in 2012 and ended its renewal in March 2021. Using this database, we analyzed the treatments used for patients with Crohn’s disease (CD), and the association of the treatments with clinical phenotypes.

Methods: In total, 262 patients with CD were registered. Of these, 154 cases that had completed records of small intestinal evaluation and registration of treatments were enrolled. Treatments received within 6 months after diagnosis were evaluated.

Results: Among the registered patients, 137 (89.0%) received enteral nutrition, whereas only 68 (44.1%) patients received exclusive enteral nutrition. Mesalazine was used in 124 (80.5%) patients, and oral or intravenous steroids were used in 50 (32.5%) patients. Immunosuppressants and anti-tumor necrosis factor (TNF) agents were administered in 56 (36.4%) and 50 (32.5%) of the patients, respectively. None of the registered patients received ustekinumab or vedolizumab within 6 months after diagnosis. As for anti-TNF agents, infliximab and adalimumab were used in 32 and 21 patients, respectively; there was no significant difference in age of onset in the two treatment groups (11.8 and 12.2 years old, respectively). Combination therapy with thiopurines was performed in 14 (43.8%) and 4 (19.0%) of infliximab- and adalimumab-treated patients, respectively. In terms of clinical phenotypes, L1 disease was associated with less use of steroids, and perianal disease was associated with significantly less use of steroids and greater use of anti-TNF agents (p<0.05, chi-square test). Growth failure, upper gastrointestinal involvement (L4 location in Paris classification), and disease behavior (B1/B2/B3 phenotypes in Paris classification) were not associated with any particular treatment.

Conclusions: The registry data have clarified current treatments for pediatric CD patients in Japan. Mesalazine and enteral nutrition were used in most of the patients. Patients with perianal lesions are more likely to receive anti-TNF treatments.
P-061

Real-Life Experience of Anti-drug Antibodies Against Anti-TNF Agents at Two Tertiary Care Paediatric Inflammatory Bowel Disease Centres

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Objectives and Study: Anti-tumour necrosis factor (anti-TNF) agents are increasingly used in moderate to severe paediatric inflammatory bowel disease (IBD). However, a subset of children develop anti-drug antibodies (ADA) against these agents, which can result in worsening symptoms, decreased mucosal healing, and ultimately even to progression to bowel resection. Data on the optimal management and predictive factors of ADA, are not yet determined in paediatric IBD. Therefore, we aimed to evaluate treatment interventions to overcome ADA in children with IBD. Secondary aim was to investigate predictive factors of ADA development.

Methods: In this retrospective cohort study, children 4-18 years old, diagnosed with IBD and were prescribed anti-TNF agents including infliximab and adalimumab between January 2006 and November 2021, were included in two tertiary centres. Primary outcome was the suppression of ADA (<12 AU/mL) after treatment intervention, comprising dose optimisation, switch to another anti-TNF agent, adding an immunomodulator (IM) or alternative treatments in ADA positive children. Secondary outcomes included predictors of ADA development. These predictive factors were tested by using Cox proportional-hazards model.

Results: A total of 298 paediatric IBD patients (215 Crohn’s disease; 71 ulcerative colitis; 12 IBD-unclassified) on anti-TNF therapy (288 infliximab; 10 adalimumab) were included. Fifty-seven patients (19.1%) developed ADA after a median time of 16.4 months (IQR 7.0 – 25.2) following initiation of anti-TNF treatment: 51 to infliximab and 6 to adalimumab (after a switch from infliximab for other reasons than ADA). Total duration of treatment on anti-TNF agents for the 298 patients was 885 person-years. The incidence rate of ADA was 6.44 per 100 person-years. The interventions to overcome ADA and the effect on ADA suppression is depicted in Table 1. In the group of patients with ADA <50 AU/mL (n = 31), 20 patients continued on the initial anti-TNF agent (dose optimisation, IM addition, or both). Of these patients, 90% and 80% had suppressed ADA and sustained treatment response at 6 and 24 months, respectively. In patients with high ADA levels >50 AU/mL (n = 26) who underwent dose optimisation (n = 6), IM addition (n = 1) or both (n = 4), 45% and 36% of subjects had ADA suppression and continued on the initial anti-TNF agent at 6 and 24 months, respectively. The development of ADA against anti-TNF was positively associated with female sex (hazard ratio [HR] 2.22, 95% CI 1.27 – 3.85, P = 0.005) and the presence of infusion reactions (HR 2.94, 95% CI 1.59 – 5.44, P = 0.001).
Table 1. Interventions to suppress anti-drug antibodies to anti-TNF agents in children with inflammatory bowel disease

<table>
<thead>
<tr>
<th>Type of intervention</th>
<th>ADA level ((UE/mL)), median (IQR)</th>
<th>Patients with ADA tested after intervention, (n)</th>
<th>Median days (IQR) from ADA until subsequent ADA test</th>
<th>ADA suppressed</th>
<th>ADA not suppressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continued on same anti-TNF agent ((n = 33))</td>
<td>31 (24 – 115)</td>
<td>30*</td>
<td>84 (56 – 156)</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td>• Dose optimisation ((n = 20))</td>
<td>31 (24 – 94)</td>
<td>17*</td>
<td>84 (55 – 116)</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>• IM added ((n = 3))</td>
<td>40</td>
<td>3</td>
<td>156 (56 – 500)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>• Both ((n = 8))</td>
<td>52 (21 – 170)</td>
<td>8</td>
<td>75 (55 – 160)</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>• Watchful waiting ((n = 2))</td>
<td>26</td>
<td>2</td>
<td>498 (495 – 500)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Switch to alternative anti-TNF agent ((n = 16))</td>
<td>160 (50 – 468)</td>
<td>10**</td>
<td>175 (87 – 313)</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>34 (16 – 80)</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

- ADA, anti-drug antibodies; IM, immunomodulator
- * switched to alternative anti-TNF agent prior to second test \((n = 2)\), second test >2 years after intervention \((n = 1)\)
- ** surgery \((n = 2)\), second test >2 years after intervention \((n = 3)\), lost to follow-up \((n = 1)\)

**Conclusions:** In this real-life cohort of children with IBD, around 20% of patients developed ADA against anti-TNF agents. Our data suggest that dose optimisation and/or IM addition for low-level ADA (<50 AU/mL) is an effective intervention to suppress ADA and prevent loss of response, while this was effective in only one-third of patients with high ADA (response at 24 months). Female sex was predictive of ADA development. A more sex-specific approach might therefore be considered to lower the risk of ADA in female patients.
Suboptimal vaccination coverage and serological screening in West Australian children with Inflammatory bowel disease- an opportunity for improvement.

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Objectives and Study: Despite a well-defined screening pathway prior to starting immune-suppression(IS) and vaccination guidelines, several retrospective studies have reported incomplete vaccination and screening in patients with Inflammatory Bowel Disease(IBD) but there are limited prospective data. Our objectives were to assess vaccination coverage of children attending IBD clinics using prospectively recorded Australian immunisation register (AIR).

Methods: Australian Immunisation Register(AIR) is a national register that prospectively records all vaccinations given to all people in Australia. Accuracy of vaccination-related data capture and transfer AIR has been previously established. Data from the (AIR) were audited for recommended age-appropriate routine and additional recommended vaccinations (23 valent Pneumococcal, third dose of Human Papillomavirus(HPV), and yearly Influenza) in children with IBD, attending Perth Children's Hospital, Western Australia. In addition to AIR, electronic medical records were examined to check compliance with serologic testing for Quantiferon TB, Hepatitis B, Hepatitis C, Varicella, and EBV serology prior to commencement of IS (Conventional immunomodulators (IM) -Methotrexate(MTX)/Azathioprine(AZA)/Tacrolimus/(TAC) and/or Biologics). Demographic details including age, sex, disease classification, and therapy exposures were recorded. Patients on Nutritional therapy, a single course of prednisone/budesonide, or Amino salicylates were defined as non-IS groups.

Results: 243(140-Males) with Crohn's disease(n=120), Ulcerative colitis (n=106), and Inflammatory Bowel disease unclassified (n=17) were included for analysis. 181/243(74.5%) were exposed to immune-suppressants (IS) including biologics-26%(47/181, (conventional IM)-25%(45/181) and 49%(90/181)combination of Biologics with IM. Incomplete coverage for age-appropriate routine vaccinations was 71/243(29.2%), with similar incomplete coverage between IS vs. non- IS group(56/181vs.15/62, p=0.3). Incomplete coverage of routine individual vaccines were; HPV 24%(49/203), Varicella 16%(39/243) & DTP 6.5%(16/243) Figure1. Coverage for additional recommended vaccinations for eligible children on IS was 1.6%(3/181) Pneumococcal 23 Valant, 22.8%(36/158) for the third dose of HPV, and 80%(145/181) annual influenza vaccinations. Screening prior to commencing IS was 13.2%(24/181) EBV, 67%(122/181) Quantiferon TB,64.5%(117/181) for hepatitis B and C serology, and 74.6%(135/181) for varicella IgG.
Conclusions: Our audit of the Australian Immunisation register highlights that almost 30% of children with IBD were noncompliant with their routine recommended vaccination. Coverage of additional recommended vaccines while on immune suppression was also disappointingly low at 3% for 23 Valant Pneumococcal, 23% for the third dose of HPV, and 80% for any influenza vaccine. Screening prior to commencing IS was suboptimal in our IBD cohort, with almost one-third of patients not having a record of Quantiferon TB, Hepatitis B, C serology, and Varicella IgG. This audit highlights the need for improved awareness and access to specialised vaccination clinics to enable vaccination coverage of immunocompromised children with IBD.
Safety and efficacy of granulocyte-monocyte apheresis in paediatric ulcerative colitis

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Objectives and Study: Granulocyte-monocyte apheresis (GMA) allows depuration of activated granulocytes and monocytes that participate in inflammatory processes. Safety and efficacy of GMA have been proven but its role in paediatric ulcerative colitis (P-UC) is not clear. Our goal was to describe the current uses and evaluate the results of GMA in our cohort.

Methods: Observational retrospective cohort study of P-UC patients who underwent GMA sessions. Demographic, clinical, and analytic variables were analysed at week 0, week 5, 6 months and 12 months after starting GMA. Session schemes where analysed and classified according to their indication into concomitant, co-adjuvant, or maintenance therapy. Clinical remission was defined as a PUCAI < 10 points.

Results: Nine patients were analysed (5 were male; the median age at beginning of GMA was 15.7 years [IQR 15.3-16.9]). Group A included 5 patients that received GMA as concomitant or bridge therapy after starting biologic treatment (4 Vedolizumab, 1 Ustekinumab). Group B included 1 patient that received GMA as co-adjuvant treatment due to partial response to anti-tumour necrosis factor (anti-TNF). Group C included 3 patients that received GMA as maintenance therapy due to intolerance to or presenting side effects of azathioprine. The median time from diagnosis to beginning of GMA was 2.86 years (IQR 1.19-8.04), and the median duration was 41.6 weeks (IQR 6.9-62.3). Session schemes were diverse, the most frequent was 1-2 weekly sessions for the first 10 sessions, followed by sessions every 1-4 weeks for 6-12 weeks, with posterior maintenance with monthly or bimonthly sessions. The median PUCAI score before GMA in group A was 55 (IQR 37.5-80), in group B 20, and in group C 0. The full cohort analysis revealed a significant decrease in PUCAI (-25.7 points [p 0.05]) at week 5, but not at 6 or 12 months. In group A 80% (4/5) had a decrease in PUCAI by week 5 (p0.71) and one patient (20%) achieved clinical remission by month 12 while on concomitant treatment with Vedolizumab maintenance therapy with GMA. The patient in group B achieved sustained clinical remission since week 5. In group C patients started GMA on clinical remission and sustained it during maintenance therapy. There was a significant improvement in haemoglobin by week 5 (p0.03), month 6 (p0.013), and month 12 (p0.05) in the full cohort analysis. The rest of blood parameters did not show significant improvement. Four out of nine patients required therapeutic escalation after beginning GMA. Two patients in group A required colectomy, one of them before the start of GMA and the other after receiving GMA. Two patients (22%) presented mild complications related to catheter infections.

Conclusions: GMA is a safe therapeutical strategy in different clinical scenarios in P-UC. Despite the scheme variability in our cohort, we evidenced a significant decrease in inflammatory activity in the short term. GMA proved to be effective in maintaining clinical remission, especially in patients with intolerance or side effects to immunosuppressors.
Phosphomannomutase 2 (PMM2) variants leading to Hyperinsulinism-Polycystic Kidney Disease are associated with Early-Onset Inflammatory Bowel Disease and gastric antral foveolar hyperplasia

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Objectives and Study: Phosphomannomutase 2, encoded PMM2, is a non-redundant component of the N-glycosylation pathway, responsible for the post-translational modification of a diverse array of proteins. Biallelic deleterious variants in PMM2 underlie the commonest Congenital Disorder of Glycosylation (CGD) disease (CGD-1a, or CGD-PMM2). We recently reported a cohort of patients affected by hyperinsulinaemic hypoglycaemia (HI) and autosomal recessive polycystic kidney disease (PKD - HIPKD) and identified a specific underlying variant in the promotor of PMM2, which was found either in homozygosity or in trans with deleterious variants in PMM2. Here we report that three of these patients have additionally developed Inflammatory Bowel Disease (IBD) in childhood, and manifest a distinctive pattern of gastric antral disease involvement.

Methods: We report a clinical case series of three patients. Reanalyses of published intestinal transcriptomic datasets support hypothesis generation around potential mechanism(s) of association.

Results: Patient 1 presented at 6 months of age with bloody diarrhoea and was found to have moderately-severe, non-granulomatous, chronic active inflammation in the oesophagus, stomach, duodenum, and throughout the colon. HI and PKD were identified at 13, and 17 months, respectively. Gastrointestinal (GI) symptoms abated and by 5 years of age he was able to stop all anti-inflammatory medications. However gastric antral abnormalities were persistently evident, with the development of foveolar hyperplasia and a hyperplastic polyoid appearance.

Patient 2 had an antenatal diagnosis of PKD and developed symptomatic HI in the first few days of life. At 10 years of age he developed bloody-mucoid diarrhoea and was found to have patchy gastric antral redness, corresponding with foveolar hyperplasia, in addition to moderately-severe, non-granulomatous, chronic active pancolitis.

Patient 3 had HI and PKD identified in the first few days of life. At 6 years of age he developed watery and mucoid diarrhoea and was found to have eosinophilic oesophagitis, patchy redness in the gastric antrum with foveolar hyperplasia and mild-moderately-severe patchy left-sided chronic active colitis. The patients all carry the promoter variant in PMM2 (c.-167G>A)in trans with a pathogenic variant. The tissue specificity of disease manifestations (which is in contrast to that seen in CGD-PMM2) is proposed to result from the promotor mutation destabilising a chromatin loop that facilitates activity of a cis-acting regulatory element, HNF4a: organ-level expression of HNF4a directly corresponds with disease manifestations. Reanalysis of single cell data suggests that this condition is likely to represent an epithelial defect. In the stomach, it may relate to dysregulated isthmus cell proliferation.

Conclusions: PMM2 gene defects can cause early-onset inflammatory bowel disease and thus may represent a novel Mendelian cause of IBD, albeit with low penetrance (10% (95% CI 3.5-25.6)). Although the mechanisms underlying this association are undefined, based on gene expression data we propose that PMM2-related HIPKD-IBD likely represents an epithelial-intrinsic defect.
An international prospective study of the paediatric IBD incidence: current trends and findings

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Objectives and Study: The incidence of paediatric-onset inflammatory bowel disease (PIBD) remains unclear in several European and non-European countries. Subsequently, the factors that may drive the incidence of PIBD also remain unknown. We designed an international prospective study, which allows us to calculate PIBD incidence using exactly the same methodology in multiple countries and regions. With this study, we aimed to determine the incidence of PIBD and reveal important trends over time and between regions, populations, and several populations that have been exposed to different environmental factors.

Methods: An electronic survey system based on the REDCap database was launched in 2017 to capture the referral and patient population of PIBD experts in 30 countries. In the currently ongoing study, PIBD experts are invited to complete an annual survey that collects data regarding the location and type of clinical service, and the number of new and current cases of PIBD in their service. Each respondent also answers data validation questions and identifies the areas their patients are mainly referred from (regional coverage). A key element for our calculations in Europe is the use of the Nomenclature of Territorial Units for Statistics (NUTS) as defined by Eurostat. This structure allows us to combine the collected regional PIBD data with the more than 5000 validated datasets that are available in the Eurostat and European Environmental Agency databases, including the populations of children within each area as defined by the respondents.

Results: Over the 5 years of the study, we have gathered responses from over 200 paediatric gastroenterologists covering over 100 million person-years and 6,778 PIBD patients in 30 countries (5 in Asia, 2 in North America & 23 in Europe). Specifically for the UK and the Netherlands, the coverage since 2017 has exceeded the 85% and 90% of the total paediatric population respectively and presented consistent and yet increasing incidence figures over time:

<table>
<thead>
<tr>
<th>Year</th>
<th>PIBD Incidence in the UK per 10^5 (95% CI)</th>
<th>PIBD Incidence in the NL per 10^5 (95% CI)</th>
<th>PIBD Incidence in all regions per 10^5 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>6.5 (5.9–7.4)</td>
<td>5.6 (4.8–6.5)</td>
<td>5.7 (5.2–6.2)</td>
</tr>
<tr>
<td>2018</td>
<td>Not collected</td>
<td>Not collected</td>
<td>Not collected</td>
</tr>
<tr>
<td>2019</td>
<td>9.6 (8.3–11.0)</td>
<td>5.9 (5.1–6.7)</td>
<td>6.1 (5.8–6.4)</td>
</tr>
<tr>
<td>2020</td>
<td>10.0 (9.3–10.7)</td>
<td>6.3 (5.7–6.9)</td>
<td>6.2 (6.0–6.5)</td>
</tr>
<tr>
<td>2021</td>
<td>11.1 (10.2–12.1)</td>
<td>6.8 (5.9–7.9)</td>
<td>6.6 (6.3–7.0)</td>
</tr>
</tbody>
</table>

Overall, in Europe, we have detected a strong latitude effect with countries in the north (above 50 degrees of latitude) reporting a 2-fold increase in the incidence compared to the countries in the south (below 42 degrees of latitude) and a 1.5-fold increase compared to the countries in between. In multiple spatial regression analysis, we have identified sun exposure as one of the main predictors that explain almost all the variance that we observe as the latitude changes while we have also identified a strong correlation of the incidence with other diseases and certain pollutants (analysis ongoing).

Conclusions: This study has shown our ability to obtain the incidence of PIBD prospectively, in multiple countries in a uniform manner, presenting consistent results compatible with previous data, through a very large referral population. Our data allow direct comparisons between different regions, data collection years and the study of the effects of several environmental factors. The results suggest a rapid increase in the PIBD incidence worldwide. The United Kingdom and the Netherlands were the 2 countries with the highest population coverage in our study and reported a steady, linear increase of 1.1 (95% CI: 0.81–1.45) and 0.3 (95% CI: 0.17–0.41) additional new cases per 10^5 paediatric person-years respectively.
Usefulness of 5-ASA in the maintenance treatment of pediatric Crohn disease

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**Objectives and Study:** Current therapeutic options for active Crohn disease (CD) aim to achieve remission. Once achieved, maintenance of surgically induced or medically induced CD remission is a key therapeutic goal. There are conflicting results on the role of 5-ASA in the maintenance treatment of Crohn’s disease, which are attributed to heterogeneous research subjects, differences in the types and doses of drugs, and different research design. The aim of this study is to evaluate the effectiveness of 5-ASA in maintaining medically induced Crohn’s disease remission.

**Methods:** A single-center retrospective study of 40 pediatric Crohn patients who were administered 5-ASA as a maintenance therapy with 1-year minimum follow-up between 2005 and 2016 was conducted. Data regarding patient demographics and comparison of characteristics of patients receiving 5-ASA or other drugs were collected. CD phenotype at diagnosis was assessed using the Paris Classification. Long-term outcome is defined as prolonged response (still in complete/partial response 1 year after induction of response). Poor medication adherence is defined as medication skip more than 1 month or taking medicine less than 2/3 of dispensed prescription drugs.

**Results:** Of 144 people in total, number of patients receiving 5-ASA, anti-TNF or non-biologics besides 5-ASA as a maintenance therapy was 40 (27.8%), 75 (52.1%) and 29 (20.1%), respectively. Mean follow-up duration was 5.20±3.85 years. Patients receiving 5-ASA had a higher rate of B1 \((P=0.036)\), small bowel only involvement \((P=0.02)\), and poor medication adherence \((P=0.019)\) compared with patients receiving other drugs as a maintenance therapy. Patients receiving 5-ASA had a lower rate of number of follow-up colonoscopy \((P=0.005)\), diarrhea \((P=0.049)\), L3 \((P=0.007)\), and B2 \((P=0.046)\). Mean age at diagnosis, family history of IBD, and accompanying symptoms (abdominal pain, weight loss, fever, and hematochezia) were not significantly different between the two groups. Endoscopic relapse rate in patients receiving 5-ASA was 10%.

**Conclusions:** Twenty-eight percent of patients obtained long-term benefit in maintaining medically induced Crohn’s disease. A selected phenotype of Crohn’s disease patients may profit from 5-ASA.
P-067

Epidemiologic Study of Paediatric Inflammatory Bowel Disease according to Age Subclassification: Nationwide Population-Based Study in Korea

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Objectives and Study: Paediatric inflammatory bowel disease (PIBD) shows various phenotypes according to age. We aimed to investigate the age and sex standardised incidence rate (SIR) including temporal trends and regional differences of PIBD in Korea in the subsets of age groups using the nationwide population-based database.

Methods: We analysed data from the National Health Insurance Service (NHIS) of the Korean government and the Korean Statistical Information Service from 2005 to 2016. We divided the age at diagnosis into infantile-onset (IO, 0-1 year), very early-onset (VEO, 2-5 years), early-onset (EO, 6-9 years), and later-onset (LO, 10-16 years). Study regions were divided into metropolitan and non-metropolitan areas. The overall and annual SIRs were analysed. Temporal trends and regional difference of SIR between metropolitan and non-metropolitan areas were analyzed using linear Poison regression analysis.

Results: From 2005 to 2016, 2,734 incident cases (1,815 males and 919 females) were diagnosed with IBD before the age of 17 years. In the overall population, the SIR of PIBD over the entire study period was 2.248/10⁵. It was increased from 1.001/10⁵ in 2005 to 3.701/10⁵ in 2016. The SIR of IO-PIBD was 0.227/10⁵ in 2005 and 0.000/10⁵ in 2016 (p= 0.611). The SIR of VEO-PIBD was 0.192/10⁵ in 2005 and 0.268/10⁵ in 2016 (p= 0.17). The SIR of these two groups remained stable. On the other hand, the SIR of EO-PIBD increased from 0.079/10⁵ in 2005 to 0.683/10⁵ in 2016 (p= 0.022) and that of LO-PIBD increased from 2.052/10⁵ in 2005 to 7.744/10⁵ in 2016 (p < 0.001) (Figure-(a)). In paediatric Crohn’s disease (PCD), the SIR of LO-PCD showed an increasing trend (p < 0.001), but the SIRs of IO-PCD (p= 0.084), VEO-PCD (p= 0.068), and EO-PCD (p= 0.331) remained stable (Figure-(b)). In paediatric ulcerative colitis (PUC), the SIR of LO-PUC (p= 0.021) and EO-PUC (p= 0.033) increased, while the SIR of IO-PUC(p= 0.243) and VEO-PUC (p= 0.806) remained stable (Figure-(c)). The SIRs of EO-PCD and LO-PCD showed a difference between metropolitan and non-metropolitan areas, while the SIRs of IO-PCD, VEO-PCD, and PUC of all age groups showed no statistical difference.
**Conclusions**: Our study showed that the SIR of LO-PIBD and EO-PIBD increased whereas those of IO-PIBD and VEO-PIBD remained stable in Korea. The SIR of EO-PCD and LO-PCD showed a regional difference between metropolitan and non-metropolitan areas. Our results suggest that genetic factors are more likely to play a role in the development of IBD at younger ages.
The incidence of the paediatric inflammatory bowel disease and the use of biological treatment have increased during the Covid-19 pandemic in NE Slovenia

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Objectives and Study: It has been shown that the incidence of paediatric inflammatory bowel disease (IBD) is rising. Also, the use of biological treatment has become more common, partly due to the newest recommendation by the European Crohn’s and Colitis Organization. Stress can be one of factors associated with exacerbations of IBD. Covid-19 pandemic has become an important psychological burden for children and adolescents.

The aim of our study was to assess the incidence of IBD and the use of biological treatment in IBD patients in the NE Slovenia during the ten-year period. Also, we studied whether the incidence of paediatric IBD and the use of biological therapy have changed during the Covid-19 pandemic.

Methods: A retrospective, single centre observational study was conducted in a cohort of children and adolescents (<19y) diagnosed with IBD between 2012 and 2021 in NE Slovenia. The observed time interval was divided into a pre-Covid-19 period (period one: 2012-2015 and period two: 2016-2019) and Covid-19 period (2020-2021). Annual incidence rates of Crohn’s disease (CD) and ulcerative colitis (UC) were calculated. Further, the number of IBD patients requiring biological treatment was determined. The time interval between the confirmation of the diagnosis and the start of biological therapy was calculated and compared between chosen time periods and between disease groups.

Results: During the study period, 71 IBD patients (46% male, mean age 15 years, 58% UC) were diagnosed in NE Slovenia. Mean annual incidence of IBD (per 100.000) was 5.2 (95 % CI 3.4-7.1; CD 2.2 (95 % CI 1.0-3.6), UC 3.0 (95 % CI 2.1-3.9); NS). During the Covid-19 period the incidence of IBD has risen significantly (p<0.05) compared to the previous two periods (9.1 vs 4.2 respectively) (Figure 1). More than one third of patients (N=27; 52% male, mean age 14 years, 52% UC) have been switched to the biological therapy during the study period. The median time interval from the confirmation of the diagnosis to the start of the biological therapy was 12 months (IQR 4-35m; CD 7m, UC 14.5m; NS). There was significant difference in time from diagnosis to biological treatment according to the study period, with the interval being the shortest during Covid-19 period (6m), compared to period one (38m; p<0.05), and period two (17m; NS). 14 patients (64% male, mean age 15 years, 50% UC) have been switched to biological treatment within one year from the diagnosis. The percentage was the highest in the Covid-19 period compared to period two and one (88% vs 22% vs 0%; p<0.05).
Conclusions: The incidence of IBD in NE Slovenia has increased significantly in the last ten years, especially during the Covid-19 pandemic. Ten years ago, the incidence of UC was higher than CD, however, the ratio between CD and UC has equalized during the Covid-19 period. Also, the number of patients that were switched to the biological therapy within one year after the conformation of diagnosis has increased significantly in the Covid-19 period, which might be due to new guidelines for diagnosing paediatric IBD and possibly also to the change of the lifestyle during the Covid-19 pandemic.
Early anti-TNF therapy results in higher sustained steroid free remission rates in children with newly-diagnosed Crohn’s disease: a prospective observational cohort study


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Objectives and Study: For paediatric Crohn’s disease (CD) patients with a high risk of complicated disease (B2 [stricturing] and/or B3 [penetrating] disease), guidelines recommend early anti-tumor necrosis factor-alpha (anti-TNF) therapy, as this has been demonstrated to halt disease progression. The role of early anti-TNF therapy in achieving medium-term targets, such as sustained steroid free remission (SSFR) is yet to be investigated. In this prospective inception cohort study, we aimed to evaluate outcomes of disease at 1 year in paediatric CD patients, and to evaluate the role of early anti-TNF therapy.

Methods: Since January 2017, children (0-18 years) with newly diagnosed CD were prospectively enrolled in the PIBD-SETQuality inception cohort study in 28 international centers. Demographic and clinical data were collected at baseline and at 1, 3, 6 and 12 months. The primary outcome was SSFR at 1 year (defined as a weighted Paediatric CD Activity Index <12.5 without steroids between 3 and 12 months) without treatment escalation. Secondary outcomes included biochemical remission (remission with faecal calprotectin <300 mcg/g or CRP < 5 mg/l), steroid free remission (SFR) at 3 and 12 months, and need for intestinal surgery. Outcomes were compared between the early anti-TNF cohort (Infliximab [IFX] or Adalimumab [ADA]) within 90 days after diagnosis) and the no early anti-TNF cohort.

Results: Up to April 2022, 418 children with newly-diagnosed CD were included of which 274 completed at least 1 year of follow-up (61% male, median age at diagnosis 13.8 years [IQR 11.6-15.2]). In total, 108 (39.4%) patients were treated with early anti-TNF (57% IFX, 43% ADA; median time to start after diagnosis 16 days [IQR 9 – 47] for IFX, 50 days [IQR 21 – 70] for ADA). The early anti-TNF cohort had higher rates of moderate-to-severe disease at baseline than the no early anti-TNF cohort (73% vs. 63%, p=0.10). While 61% of all patients were in SFR at 1 year, only 57/257 (22%) were in SSFR at 1 year. Six patients had required treatment escalation (1 in early anti-TNF cohort), resulting in 51/257 (20%) patients in SSFR without treatment escalation. Rates of SSFR without treatment escalation were higher in the early anti-TNF cohort (30/103 [29%] vs. 21/154 [14%], p=0.002). At 3 months, the early anti-TNF cohort also had higher rates of SFR (54% vs. 40%, p=0.034), normalized CRP (80% vs. 54%, p<0.001), and normalized fecal calprotectin (54% vs. 24%, p=0.009), suggesting a deeper level of induced of remission. Of those patients in SFR at 3 months, 51/110 (46%) achieved SSFR at 1 year without treatment escalation, which did not significantly differ between the early anti-TNF cohort (30/54 [56%]) and the no early anti-TNF cohort (21/56 [38%], p=0.06). Twelve patients (4.4%) required luminal resection within the first year (6 in both groups).

Conclusions: Paediatric CD patients treated with early anti-TNF had higher chances of achieving SSFR without treatment escalation at one year than those started on other immunosuppressive treatment. This might be caused by better short-term response of early anti-TNF. This study highlights the importance of initial response to induction treatment. Future studies should identify those patients that require early anti-TNF therapy to minimize risk of complications as a result of disease progression.
Anti-tumor necrosis factor alpha therapy withdrawal in paediatric patients with inflammatory bowel disease: a prospective observational study


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Objectives and Study: Anti-tumor necrosis factor alpha (anti-TNF) therapy has revolutionized the treatment of paediatric inflammatory bowel disease (IBD). Given the impact of anti-TNF therapy on patient’s daily life and societal costs, adverse side effects such as skin reactions, and the potential risks of complications such as severe infections or cancer, withdrawal from anti-TNF could be favorable in a group of patients in sustained clinical remission (SCR). Data on number of patients in SCR with ongoing anti-TNF, and outcomes after withdrawal are scarce. Because of this, and fear of relapse after withdrawal, ceasing anti-TNF is hardly done in children. We aimed to investigate rates, indications and outcomes after discontinuation of anti-TNF in children with IBD, and to characterize patients in SCR in whom anti-TNF withdrawal might be considered.

Methods: We conducted a multicenter prospective inception cohort study (PIBD-SETQuality) of children (age 0-18) with newly-diagnosed IBD and selected patients with at least 1 year of follow-up who ever received anti-TNF therapy. Two cohorts were analyzed separately: 1) in the anti-TNF withdrawal cohort, consisting of patients that ever ceased anti-TNF (Infliximab [IFX] or Adalimumab [ADA]), we assessed rates and indications for withdrawal and sequelae after discontinuation; 2) in the anti-TNF maintenance cohort, consisting of patients with ongoing anti-TNF for at least 6 months at their last follow-up visit, we compared disease characteristics and therapy details between patients in SCR or patients without SCR, which was defined as remission by disease activity score or as quiescent disease during the past 6 months.

Results: From January 2017 to January 2022, 685 patients were enrolled in the study of which 444 had at least 1 year of follow-up (274 Crohn’s disease; 59% male; median age at diagnosis 13.7 years [IQR 11.1 – 15.2]). Of these, 280 (63.1%) had ever received anti-TNF therapy (median follow-up duration 101 weeks [IQR 74 – 116]). Withdrawal of anti-TNF occurred 63 times (49 IFX, 14 ADA) in 58/280 (20.7%) patients, after a median duration of 28.0 weeks (IQR 12.5 – 45.8) for IFX and 23.5 weeks (IQR 15.3 – 48.0) for ADA. Frequently reported indications for withdrawal were loss of response (n=18), primary non-response (n=10), adverse effects (n=8), and development of antibodies (n=5; all to IFX). Only 4 patients ceased anti-TNF because of SCR. A total of 204 patients had ongoing anti-TNF for at least 6 months (117 IFX, 87 ADA), of which 116/195 (59.5%) were in SCR. There were no significant differences in anti-TNF type, IBD type, age at diagnosis or baseline disease severity between patients in SCR and those not in SCR. None had recent endoscopy to assess mucosal healing. In Crohn’s disease patients, 44% of patients in SCR, compared to 52% of patients not in SCR, had concomitant immunomodulator use at their last follow-up.

Conclusions: While a majority of paediatric patients with IBD achieve SCR while on anti-TNF maintenance therapy, withdrawal from anti-TNF because of SCR remains rare. Endoscopic assessment of residual mucosal inflammation could aid physicians in selecting those patients in whom withdrawal of anti-TNF might be considered. Ongoing collection of real world data is needed to gain insight in outcomes after anti-TNF withdrawal, since guidelines lack evidence-based exit strategies.
P-071 (Poster of distinction)

A novel dual-company master protocol for the study of IL-23 inhibitors in pediatric Crohn’s disease

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Objectives and Study: Approvals for biologics in pediatric IBD have lagged 6-8 years behind the adult approvals. As the number of products with pediatric study requirements increases, trials will be more difficult to enroll, leading to further delays in access to safe and effective drugs for pediatric IBD patients. The use of master protocols is among the potential solutions, provided that use would improve enrollment or reduce the required sample size. Janssen and Lilly decided to work together towards formulating a master protocol for the study of IL-23 inhibitors in pediatric Crohn’s disease, incorporating an innovative Bayesian analysis.

Methods: Janssen established a GitHub® site for collaborative coding and an external-facing SharePoint® site for document management and storage. A confidentiality agreement was put in place covering limited information such as IND numbers and developmental timelines, as the platform modeling used publicly available data. Janssen and Lilly developed and submitted
(1) a meeting request for the FDA Complex Innovative Design program,
(2) a briefing package to the EMA Scientific Advice Working Party,
(3) FDA Type C meeting request and briefing package, and
(4) request for clarifications and responses to the advice received from both FDA and EMA.
Confidentiality was maintained by submitting the Investigator Brochures under separate cover (EMA) and cross-referencing the company specific INDs (FDA). Discussions of the legal and operational structure took place in parallel with development of the protocol. Advice from FDA indicated that the master protocol could be submitted to the same IND as each ISA.

Results: The master protocol covers the screening and randomization process into one of the two Intervention-Specific Appendices (ISAs). To ensure the comparability of the populations enrolled in each ISA, the master protocol includes the inclusion and exclusion criteria. Study participants are followed according to the schedule of activities (SOA) of the ISA to which they have been randomized. The SOAs of the two ISAs were harmonized to reduce a perceived difference in the burden of participation, as assignment to each ISA is not blinded. The platform-level analysis is based on the endpoint of clinical remission and endoscopic response at Week 52. Thus, the companies worked together to harmonize definitions of disease activity, responder and loss of response, rescue medications and exit criteria. As there will be no sharing of data between companies, the program will be run by an independent Contract Research Organization, with an independent statistics group performing the Bayesian analysis.

Conclusions: Master protocols may streamline clinical development in pediatrics by utilizing shared control groups, creating efficiencies in clinical operations, and reducing the number of patients required to participate in trials through innovative analytical methods. Building the collaborative infrastructure for the design and implementation of pediatric master protocols would benefit the movement toward wider use and acceptance. The ultimate goal would be to reduce the delay in pediatric approvals so that children have access to safe and effective medications in a timelier manner.
Mucocutaneous Manifestations in Paediatric Patients with Inflammatory Bowel Disease

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Objectives and Study: The skin and the mucous membranes are among the most affected organ systems in patients who suffer from inflammatory bowel disease (IBD). The mucocutaneous manifestations can present as specific lesions with the same histological features as the underlying bowel disease, as associated disorders, or reactive processes to the intestinal inflammation, as well as complications of IBD itself, or side effects from IBD treatments. The objective of this study was to evaluate the prevalence of mucocutaneous manifestations in paediatric patients with IBD and to assess their association with sex, disease type and activity.

Methods: We reviewed retrospectively the medical records of all patients with IBD treated in our department in the period November 2011-November 2021. All mucocutaneous manifestations were analysed.

Results: Totally 144 children with IBD (82 with ulcerative colitis, 59 with Crohn’s disease and 3 with very early onset IBD) took part in the study. The median age of the study participants was 14 years (range: 10 months-17 years) and 51.4% of them were girls. Mucocutaneous manifestations were detected in 14.6% of our patients and 2.1% of them presented with more than one mucocutaneous manifestation. These manifestations were more frequent in boys than in girls (57.1% vs. 42.9%, \( p=0.0896 \)) and their prevalence was higher in Crohn’s disease than in ulcerative colitis (28.8% vs. 4.9%, \( p=0.0001 \)). In the most cases the lesions were associated with clinically active disease and paralleled the disease activity.

Conclusions: We found that the prevalence of mucocutaneous manifestations in paediatric patients with IBD was 14.6%. Boys with Crohn’s disease were at increased risk for development of mucocutaneous manifestations.
P-073

Treatment with Vedolizumab in Bulgarian Paediatric Patients with Inflammatory Bowel Disease - Experience of a Referral Centre

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Objectives and Study: The introduction of anti-tumour necrosis factor alfa (anti-TNFα) therapy has greatly changed the treatment paradigm in the management of patients with inflammatory bowel disease (IBD). However, anti-TNF drugs are not effective in all patients. Vedolizumab (VDZ) is anti-integrin humanized monoclonal antibody used in adult patients with IBD. Data in paediatric IBD patients treated with VDZ are still scarce.

Methods: Single centre retrospective study including all IBD patients on vedolizumab therapy treated in our department in the period September 2020 - May 2022.

Results: Totally 8 children with IBD: 5 with ulcerative colitis (UC), 2 with Crohn’s disease and 1 with very early onset IBD (VEOIBD) took part in the study. The median age of the study participants was 11.5 years (range: 4 years - 14 years) and 7 of them were girls. Five of the patients were previously treated with anti-TNFα (2 patients had severe allergic reaction to anti-TNFα, 1 was infected with tuberculosis and 2 had secondary loss of response) and three were anti-TNFα-naïve. All patients but one had immunomodulation therapy. Vedolizumab was administered to all children – 6 mg/kg at week 0, 2, 6 and then every 8 weeks. Median follow up with VDZ: 9.5 months (range: 2 months- 18 months). Clinical response at 4th dose week was observed in 7/8 (87.5%) patients, one patient hasn't reached yet 14th week. At 5th dose week VDZ level was tested in 6/8 patients the median value was 27.5 µg/ml (range: 7.9 µg/ml - 31 µg/ml). No VDZ antibodies were found. Two patients had a relapse – 4-year-old girl with VEOIBD (level at 5th dose week - 7.9 µg/ml, no VDZ antibodies) at 22nd week and 14-year-old girl with UC at 14th month (level < 1.2 µg/ml, no VDZ antibodies). Intensification was started – 10 mg/kg at 8-week period and 6 mg/kg at 4-week period respectively. No infusion reactions or serious adverse events were reported. One girl with UC had an Ebstein-Barr viral infection between the infusions with VDZ.

Conclusions: Vedolizumab was effective in 75% of the reported children. Two of the patients had loss of response – one was with VEOIBD, anti-TNFα-naïve, and one was with UC previously treated with anti-TNFα. Further studies are necessary to identify predictors of an adequate response to treatment with VDZ in order to increase its effectiveness.
P-074 (Poster of distinction)

Predicted Incidence to 2035 of Very Early-Onset Inflammatory Bowel Disease in Two Canadian Provinces: A Population-Based Study


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Objectives and Study: Paediatric-onset inflammatory bowel disease (PIBD) is increasing globally, while data on the incidence of very early-onset IBD (VEO-IBD) remain sparse. We forecast the incidence of PIBD and VEO-IBD, along with subtypes Crohn’s disease (CD) and ulcerative colitis (UC), from 2016 to 2035 using population-based data from two Canadian provinces.

Methods: Using health administrative data from Alberta and Ontario (two Canadian provinces with universal healthcare coverage; pop. 17.5 million, 49.8% of the Canadian population), we determined the annual incidence rates of PIBD (diagnosed 6 to 17 years) and VEO-IBD (diagnosed <6 years) from 2005-2016 using validated province-specific algorithms. Autoregressive integrated moving average (ARIMA) models were used to forecast incidence rates to 2035 and their 95% prediction intervals (PI). The average annual percentage change (AAPC) with associated 95% confidence interval (CI) was calculated from forecasted incidence rates using Poisson regression models. Joinpoint Trend Analysis software was used to detect changes in the AAPC from 2005-2016 and incorporated into ARIMA models when trends in incidence were non-linear. In these cases, we report the forecasted AAPCs and incidence rates as a range, including models with and without splines.

Results: Trends in existing and forecasted data, with and without splines, are depicted in Figures A (VEO-IBD) and B (PIBD). From 2016 to 2035, the incidence of VEO-IBD is forecasted to increase between 2.5% (95% CI 2.1% to 2.7%) and 2.7% (95% CI 2.9% to 4.2%) per year. The estimated incidence of VEO-IBD in 2035 will be between 6.8 (95% PI 5.3 to 8.4) and 9.3 (95% PI 7.2 to 11.3) per 100,000 person-years. The incidence of VEO-CD was forecasted to increase between 1.8% (95% CI 0.1% to 2.7%) and 2.9% (95% CI 1.8% to 3.6%) per year, while the incidence of VEO-UC is not expected to change significantly (-4.3% [95% CI -54.5% to 4.4%] to 2.1% [95% CI -1.0% to 3.4%]). The incidence of PIBD is expected to reach 33.1 (95%PI 31.7 to 34.5) per 100,000 person-years by 2035, increasing by 1.9% (95% CI 1.7% to 2.0%) per year. The incidence rates of paediatric-onset CD and UC are expected to increase by 1.5% (95% CI 0.7% to 2.1%) and 2.4% (95% CI 1.6% to 2.9%) per year.
Conclusions: The incidence rates of VEO-IBD and PIBD are expected to significantly increase through 2035, assuming past trends continue. Immigration changes could alter trends since underlying risk may be different in people from various regions. Similarly, environmental changes may either increase or decrease rates of PIBD. There is a need to ensure adequate access to high-quality specialist care for these children with the goal of minimizing the impact of their disease on their long-term disease course, quality of life and psychosocial well-being.
COVID-19 vaccine-induced antibody responses in paediatric inflammatory bowel disease patients treated with anti-TNF therapy.

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Objectives and Study: Impaired antibody responses to a single dose of the Covid-19 vaccine have been reported in adult inflammatory bowel disease (IBD) patients. However, the true impact of immunosuppressant therapies on SARS-CoV-2 vaccine efficacy in paediatric IBD patients is currently unknown. Our objective was to evaluate the immunogenicity of the COVID-19 vaccine in paediatric IBD patients treated with maintenance anti-TNF therapies.

Methods: In this single centre prospective study, paediatric IBD patients aged 5-17 years, from 1st June 2021 to 1st May 2022, treated with maintenance anti-TNF therapy, alone or in combination with an immunomodulator, who received the BNT162b2 SARS-CoV-2 vaccine were recruited. The primary endpoint was assessment of serum antibody concentrations, specifically anti-SARS-CoV-2 spike protein and receptor-binding domain (RBD) antibodies, determined at baseline and 28 days after the first and second vaccine doses and to compare paediatric results with healthy adults who had received the vaccine. The secondary outcome was to compare serum antibody concentrations in adolescent patients aged 12-17 years with antibody levels in younger children aged 5-11 years, after 2 doses. Serum antibody concentrations were assessed using V-PLEX SARS-CoV-2 Panel 2 (IgG) assay (Meso Scale Diagnostics).

Results: In total 196 participants were included (IBD patients: n=164, median age 15 years [IQR 12-16], 37% female, 70% Crohn’s disease, 27% ulcerative colitis, 3% inflammatory bowel disease unclassified, 87% Paediatric Crohn's Disease Activity Index (PCDAI) ≤10, 13% PCDAI >10-30, 53% Anti-TNF monotherapy, 47% Anti-TNF in combination with an immunomodulator (azathioprine or methotrexate), median interval between two vaccine doses 57 days (IQR 52-67); Healthy adults: n= 32, median age 36 (IQR 29-40), 65% female, median interval between two vaccine doses 46 days (IQR 42-86). After a single vaccine dose, patients on Anti-TNF monotherapy had comparable spike and RBD antibody concentrations to controls (Figure 1). In contrast, paediatric patients on Anti-TNF in combination with an immunomodulator had significantly lower antibody concentrations than controls and patients on Anti-TNF monotherapy. After two vaccine doses, there was no difference in the antibody response of patients who were on Anti-TNF monotherapy or combination therapy, compared to healthy controls (Figure 1). After two vaccine doses, adolescent IBD patients had comparable spike antibody concentrations to younger IBD children (Mean anti-SARS-CoV-2 spike protein antibody concentration 185510 AU/ml vs. 141926 AU/ml, p = 0.41).
Conclusions: Paediatric patients treated with Anti-TNF therapy in combination with an immunomodu-lator had an attenuated antibody response after a single vaccine dose. However, after 2 doses, robust antibody responses were obtained in all patients. Adolescent patients had similar antibody responses to younger children after 2 doses. This study highlights the importance of completing the COVID-19 vaccine schedule for paediatric patients on anti-TNF combination therapy. Assessment of the longevity of immune responses to SARS-CoV-2 vaccination is ongoing in our cohort.

Conflict of Interest: Kevan Jacobson: Advisory Board and Speaker Bureau: AbbVie and Jansen Sally Lawrence: Advisory Board and Speaker Bureau: AbbVie and Jansen All other co-authors: No conflicts of interest.
Prediction of relapse on thiopurine treatment: the Paediatric IBD Porto group of ESPGHAN study


Objectives and Study: According to current guidelines, most paediatric patients in Europe diagnosed with Crohn’s disease (CD) are prescribed long-term immunosuppressive therapy with azathioprine (AZA). This study aimed to develop a predictive model allowing stratifying patients who will not benefit from AZA maintenance treatment and who require a more intensive therapeutic approach early after diagnosis.

Methods: The study was designed to develop a clinical prediction rule using retrospective data analysis from patients included to prospective inception cohort, the EUROKIDS-IBD until 2017. In total, 1190 CD patients using AZA were selected from the registry in 13 European centres. Of these, 441 patients who responded to induction treatment started AZA treatment within 6 weeks from the time of diagnosis and maintained remission at week 12 were entered into this multicenter study. The primary outcome was time to clinical relapse defined as a necessity of re-induction of remission. A sequence of Cox models was fitted to predict the risk of relapse. Variables appearing to be significant in univariate risk analyses were added to the model one by one and non-significant terms were dropped.
Results:

Half of the patients did not experience clinical relapse within two years of AZA treatment initiation (figure 1). Median time to relapse was 2.11 (CI 1.59–2.46) years. Of all the tested parameters available at diagnosis, six were significant in multivariate analyses: C-reactive protein (p=0.038), body mass index Z-score >0.8SD (p=0.002), abnormal sigmoid imaging (p=0.039), abnormal oesophageal endoscopy (p=0.005), ileocolonic localization (p=0.023), and AZA dose in a specific age category (p=0.031).

Conclusions: Clinical remission was observed in 50.3% of patients after two years of AZA treatment. Although the possibility of predicting relapse on AZA treatment appears limited, we developed a predictive model based on six baseline parameters potentially useful and helpful in clinical decision.

Conflict of Interest: T.L.: reports lectures/congress fees/consultancy (outside the submitted work): Ferring, Nutricia, Biocodex, AbbVie.
M.K.: declares no conflict of interest.
J.A.D.: reports lectures/congress fees/consultancy (outside the submitted work): Rorer, Danone, Takeda, Adacyte.
M.S.: declares no conflict of interest.
S.V.B.: declares no conflict of interest.
J.M.: declares no conflict of interest.
D.E.S.: reports lectures/congress fees/consultancy (outside the submitted work): Abbvie, Dr. Reddy’s, Montavit, Nutricia, and Reckitt Benckiser, Noventure, Nestle, Nutricia.
K.W.: declares no conflict of interest.
J.S.: declares no conflict of interest.
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H.E.: declares no conflict of interest.
J.B.: reports lectures/congress fees/consultancy (outside the submitted work): MSD, AbbVie, Nutricia, Nestlé, Ferring, Biocodex, and Walmark.
Prophylactic enoxaparin fails to prevent thrombosis in high-risk pediatric inflammatory bowel disease patients

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Objectives and Study: Pediatric patients with inflammatory bowel disease (IBD) are at increased risk of developing venous thromboembolic events (VTE). Prophylaxis with low molecular weight heparin (LMWH) has been shown to decrease the incidence of VTE in adults and is widely used. Although its efficacy in preventing VTE in pediatrics has yet to be determined, it is often used in hospitalized pediatric IBD patients who are deemed high-risk for VTE. We adopted a risk-stratification algorithm to identify IBD patients at risk of thrombosis and offered LMWH prophylaxis to those who met high-risk criteria. We aimed to assess the efficacy of prophylactic LMWH in preventing VTE in high-risk hospitalized pediatric patients with IBD.

Methods: A retrospective chart review was performed at Seattle Children’s Hospital, a pediatric tertiary care hospital, from September 2012 – June 2021. Inclusion criteria were hospitalized patients with colonic IBD flares from age 0-18. Patients hospitalized for surgical procedures, isolated perianal abscess, or non-IBD colitis were excluded. VTE risk factors were personal or family history of VTE, thrombophilia, oral contraceptive or thalidomide use, smoking, obesity, or central venous line (CVL). Serious events were pulmonary embolus (PE), stroke, or cerebral sinus venous thrombosis (CSVT).

Results: 620 admissions of 417 unique patients were included. The mean age was 13.3 ± 3.9 years, with 51.3% males. 55.6% had Crohn’s disease and 41.8% ulcerative colitis. The most common risk factors were the presence of a CVL in 84 (13.5%) of admissions and obesity in 43 (6.9%). Prophylactic LMWH was used in 51 admissions (8.2%). There were 13 VTE events (2.1% of admissions); 5/51 (9.8%) in the group on LMWH and 8/569 (1.4%) without prophylaxis. The majority (8/13, 62%) were CVL-associated. Two patients had recurrent thrombi, one of whom had a diagnosis of Factor V Leiden and had 4 total events, 2 with LMWH and 2 without. There was one serious event of left middle cerebral artery thrombus leading to stroke in a patient not on LMWH. There were no serious events in the prophylaxis group. The incidence of VTE on LMWH was significantly higher than in the no LWMH group (p< 0.001, 95% CI 0.041-0.123) with RR 6.9 (p=0.003, 95% CI 1.78-24.08). Logistic regression was used to analyze the relationship between VTE and age, length of stay, disease duration, and admission labs as potential risk factors. Length of stay was a significant contributor, with an OR of 1.2 (p<0.001, 95% CI 1.096-1.342). Of the 8 VTE events that occurred without prophylaxis, only 3 had no known risk factors. Two events occurred in admissions with 1 known risk factor, and 3 in admissions with 2 risk factors.

Conclusions: Prophylaxis did not appear to prevent VTE in high-risk pediatric IBD patients. However, our risk-stratification protocol was not implemented rigorously, which may have affected results. Our population may also represent a sicker population than is common in pediatric IBD, with several patients having recurrent VTE despite prophylaxis and multiple risk factors present. An alternative prophylaxis regimen may be needed for high-risk patients. Further data is required to identify independent risk factors, and randomized control trials are needed to establish the true efficacy of LMWH in this population.

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Dr. Suskind: Chief Medical Officer and co-founder of Nimbal Health, a digital healthcare platform for IBD
Dr. Lee: None
Dr. Zheng: None
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P-078 (Poster of distinction)
Predicting pediatric IBD years before diagnosis using routine blood tests
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Objectives and Study: Recent publications have identified sophisticated markers that may help predict disease well in advance of diagnosis, with the ultimate goal of pre-disease prevention. In this population-based study, we used the epi-Israeli IBD Research Nucleus (IIRN) validated cohort to explore the utility of routine blood tests as markers for pre-diagnostic prediction of IBD in the pediatric population.

Methods: We included all blood tests for which sufficient data were available from all IBD patients insured in three of the four Israeli health maintenance organizations (HMOs), covering 49% of the population, and individually matched each to two non-IBD controls by age, sex, jurisdiction and HMO. Results of blood tests performed within the HMOs between 2003-2020 were collected and collated by number of months prior to IBD diagnosis, then reported over time until diagnosis. Means were compared using Welch’s t-test with false discovery rate correction to account for multiple comparisons. Trends over time were analyzed to detect blood tests that showed divergence between cases and controls at least one year before diagnosis.

Results: Pre-diagnosis results from 106 different blood tests were collected for 7,771 Crohn’s disease (CD) patients and 6,486 ulcerative colitis (UC) patients, including 1,539 children with CD and 767 children with UC (mean age 13.8±3.2 years for CD and 13.4 ± 4.0 years for UC). Median duration of pre-diagnosis data collection was 58 (IQR 28-110) months for CD and 56 (IQR 9-105) months for UC. Of the 106 tests, 9 (8.5%) showed significant differences between CD and controls at least one year before diagnosis; these included albumin, iron, hemoglobin, lymphocytes, mean cell hemoglobin and hemoglobin concentration, mean cell volume (MCV), platelets and red cell distribution width (RDW).

As an example, Figure 1 depicts results of albumin and MCV in children with CD (with adult data for reference); both diverged significantly from controls 19 months before diagnosis and increasingly diverged over time (cases vs. controls at 19 months pre-diagnosis - MCV: 79.1±1.3 vs. 82.4±1.1, p=0.020; albumin: 4.3±0.4 vs. 4.5±0.3, p=0.043). In UC patients, no blood tests showed statistically significant differences at least one year pre-diagnosis.
Conclusions: We were able to detect changes in routine blood tests long before diagnosis of pediatric CD. Our data opens the possibility of detecting early signals of future CD diagnosis in children undergoing routine blood tests for various reasons. These may be used for developing prediction models for prevention strategies.
This research was partially supported by the Israeli Council for Higher Education (CHE) via the Data Science Research Center, Ben-Gurion University of the Negev, Israel.
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P-079

The Effectiveness of QingDai in children with active Ulcerative Colitis

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Objectives and Study: Qing Dai (QD) is a powdered substance extracted from the leaves and roots of blue flowers, with anti-inflammatory, antioxidant, and antibacterial effects used in traditional Chinese medicine. QD has recently shown efficacy in treating psoriasis and inflammatory bowel disease. We aimed to report the effectiveness and safety of adding QD to paediatric patients with mild-moderate ulcerative colitis (UC) who failed ongoing therapy.

Methods: A multi-center retrospective study, including children (age ≤ 18) with mild- moderate UC, from 4 paediatric gastroenterology units, treated with QD between January 2017 and December 2021. Clinical, laboratory and endoscopic data were retrieved from the medical records. Disease activity was assessed by the Paediatric UC Activity Index (PUCAI) and by the physician global assessment (PGA). The primary outcome was clinical response after QD induction (up to 16 weeks from the beginning of treatment), defined as improvement of PUCAI by 10 points. Discontinuation of QD due to adverse event or lack of response, hospitalization or starting biologic treatment or corticosteroids were considered treatment failure. Fecal calprotectin (FC) levels and endoscopic MAYO scores prior to and after treatment were compared when available.

Results: 30 patients (18 males, 60%), age 12.17±3.89 years were included. Disease extent was pancolitis in 15 (54%), left sided colitis in 12 (39%), and proctitis in 2 (7%) patients (1 patient N/A). Eighteen patients (60%) were naïve to biologic treatment, and 7 (22%) received more than one biologic therapy. At the time of QD induction, 6 patients (19%) were treated with steroid, 9 (28%) with biologics (4 Infliximab, 4 Vedolizumab 4, and one Golimumab), and 13 (40%) were treated with only 5-ASA. The daily QD dose ranged from 500mg to 3000mg and was combined with 1000-4000 mg of curcumin (CurQD). The mean PUCAI decreased from 31.3±12 at baseline, to 10.9±8.8 at the end of induction (week 11.6±3.5, range 8-16) (p<0.001). Paired measurements of FC, available in 15 patients, showed a decline from a median of 749 (interquartile range (IQR)-566-1000) to 39 (IQR 12-132) at the end of induction (p=0.04). PGA, available in 24 patients, showed clinical remission in 17 (71%), clinical response in 4 (16.5%) and no response in 3 (12.5%) patients. Adverse events included headache in one patient, and haematuria in another patient, which resolved after curcumin discontinuation. Two patients (9.5%) had elevated transaminases during the maintenance treatment. The mean follow up time was 14.5±11 months. Ten patients (32%) flared while on QD treatment, one of them had spontaneous remission with no treatment change, one regained response with increased QD dose, and in 7 patients the treatment was changed. At the end of follow up, out of 18 patients with available data, 10 (55.5%) were in remission, 2 (11%) had a response and 6 (33.5%) had an active disease.

Conclusions: QD is effective and safe as an additional treatment to facilitate induction of response and remission for paediatric patients with mild- moderate UC, even after failure of biological therapy. Prospective studies are needed for further evaluating QD efficacy.
Epidemiology and changes in pharmacologic treatment of pediatric inflammatory bowel disease over 10 years in Catalonia

Loverdos I., Vela E., Brunet E., Martín de Carpi J., García Tirado D., Calvet Calvo X.

Objectives and Study: There is no data on the epidemiology of pediatric inflammatory bowel disease (PIBD) in Catalonia neither on the trends of pharmacologic treatment over time. The present study aims to evaluate the incidence, prevalence, associated morbidity and pharmacological treatment of PIBD between 2011-2020 in Catalonia.

Methods: Population-based retrospective cohort study. Children with diagnosis of PIBD (less than 18 years old) included in the Catalan Health Surveillance System database were identified using the ICD-9-CM and ICD-10-CM codes. Data on prevalence, incidence, associated morbidity and pharmacological treatment were extracted from the same database and analyzed for the study period.

Results: The pediatric population during the study period ranged from 1,369,079 in 2011 to 1,408,685 in 2020. The prevalence of PIBD rose from 27 per 100,000 inhabitants (aged <18 years old) in 2011 to 66.2 in 2020 but seems to plateau over the last 2 years of the study period. This trend was observed for ulcerative colitis (UC) (11.1 to 28.1 per 100,000 inhabitants) and Crohn’s disease (CD) (15.9 to 38 per 100,000 inhabitants). The incidence of PIBD was steadily increasing during the study period, especially for CD, and ranged from 6.8 per 100,000 inhabitants in 2011 (93 cases: 50 CD and 43 UC) to a maximum of 13.8 per 100,000 inhabitants in 2018 (193 cases: 114 CD and 79 UC). In 2019-2020 the incident cases decreased for CD and UC.

The rate of IBD related hospital admissions decreased over the study period from 244.3 per 1,000 people/year in 2011 to 112.8 per 1,000 (despite of this trend there was a peak of admissions of 257.9 per 1,1000 in 2016); while the number of outpatient clinic visits increased over the study period, from 1825 visits in 2011 to 4901 in 2020.

The percentage of patients with UC treated with systemic steroids decreased from 39.9% in 2011 to 17.9% in 2020 while the use of immunosuppressant treatment remained stable (38.6 to 30.1%). The use of biological treatment rose every year from 9.2% in 2011 to 19.9 % in 2020.

Regarding CD patients, the percentage of patients treated with systemic steroids and immune modulators decreased from 34.9% and 53% in 2011 to 12.7% and 30.2% respectively in 2020. The use of biological treatment remained stable over the study period (around 30-35%).
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<td>58</td>
<td>70</td>
<td>79</td>
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<tr>
<td>Pediatric Pop-</td>
<td>1.369.07</td>
<td>1.385.12</td>
<td>1.389.92</td>
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**Conclusions:** The prevalence of PIBD increased over the study period but seems to remain stable over the last 2 years, as the incident cases decreased in 2019-2020. It’s important to elucidate if these change of trends in PIBD has been influenced by the SARS-CoV2 pandemic or reflects a stabilization of PIBD as described in other countries. The admission rates of PIBD patients, use of systemic steroids and immunosuppressant treatment decreased (specially in UC), while the use of biologics rose.
P-081 (Poster of distinction)

Does early initiation of biologics change the natural history of pediatric Crohn’s disease? a nationwide study from the epi-IIRN

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Objectives and Study: Studies have reported conflicting findings regarding the effect of timing of biologics initiation on disease course. In this nationwide cohort study of pediatric Crohn’s disease (CD) we aimed to explore the association between time from diagnosis to biologics and disease outcomes.

Methods: Data of patients with CD diagnosed in the validated epi-IIRN cohort from 2005 to 2020 were retrieved from four Israeli Health-Maintenance-Organizations covering 98% of the population. The primary outcome was IBD-related surgery. To control for confounding by indication in which the severity of disease could account both for the timing of biologics and risk of surgery, we compared treatment strategies using the cloning, censoring, and weighting method to emulate a target trial. We created five replicates of each patient (cloning), and patients were censored at each time-point if their data were no longer compatible with their assigned treatment strategy. Inverse probability of treatment weights (IPTW) were fitted per patient to adjust by weighting for time varying confounding and selection bias. Survival curves were estimated for each strategy through weighted non-parametric Kaplan-Meier estimators. For each strategy the survival probability was evaluated at 15 years post diagnosis or last follow-up which continued into adulthood. The 95%CI for survival probabilities and differences were calculated using non-parametric bootstrap with 100 replicates.

Results: Of the 18,701 patients diagnosed with IBD, 3,406 were presented during childhood and included in the analysis. A total of 734 children initiated biologics during 0-6 month (22%), 291 during 7-12 months (9%), 176 during 1-1.5 years (5%), 208 during 1.5-2.5 years (6%), and 135 during 2.5-3.5 years (4%). The probability of surgery at last follow-up increased gradually with increased time to biologics (probability of IBD-related surgery was 0.25 [95%CI 0.13-0.37], 0.28 [0.04-0.53], 0.31[0.12-0.51], 0.33 [0.09-0.56], and 0.46 [0.17-0.75], for biologics initiation at 0-6 months, 7-12 months, 1-1.5 years, 1.5-2.5 years, and 2.5-3.5 years, respectively. The average time to surgery between the earliest and latest initiation period was 1.3 years [95%CI 0.47-2.25 p-value<0.05] (Figure).

Conclusions: Our study showed a slight advantage to earlier initiation biologics in changing the natural history of the disease, as reflected in longer time to IBD-related surgery.
No-treatment management may be a good option for a few children with ulcerative colitis - a nationwide study from the epi-IIRN

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Objectives and Study: In this nationwide study we aimed to explore the rate of non-treatment in children with UC, and their long-term outcomes.

Methods: This study was performed on data from the four Israeli Health Maintenance Organizations (HMOs), covering 98% of the population. No treatment management (NTM) was defined as lack of maintenance medical treatment for >6 months from diagnosis. Failure of NTM was defined as prescriptions of corticosteroid, 5-ASA, thiopurines, biologics or need for colectomy. Cox regression model was used to explore predictors of failure.

Results: A total of 1,752 children were diagnosed with UC in Israel since 2005, of whom, 343 (20%) patients were initially untreated, with 11,747 person-years of follow-up. NTM decreased in recent years from 22% of those diagnosed during 2005-2008 to 13% in 2017-2020 (AAPC -6.6 [95%CI -9.4 to -3.7]). The probability to remain untreated was 62%, 32% and 25% after one, three and five years from diagnosis, respectively. A one quarter of untreated PIBD (82/343 [24%]) remained without treatment until end of follow up and 177/343 (59%) remained without treatment or at most 5ASA. A total of 76 children (22%) required escalation to biologics and 24 (6.9%) required colectomy. In Cox regression model, time to failure was associated with recent year of diagnosis (HR 1.05 [95%CI 1.01-1.1]) and more severe blood tests grouped in cluster analysis (CRP, ESR, albumin, hemoglobin and WBC) at diagnosis (HR 1.4 [95%CI 1.1-2.1]). In a propensity score analysis, the outcomes of untreated patients were similar to treated patients matched by baseline characteristics, including steroid dependency [p=0.5], hospitalizations [p=0.7] and colectomy [p=0.2].

Conclusions: Nowadays, 13% of children with UC do not receive initial maintenance medical treatment and in half this step-up approach was successful. In these milder cases, the outcomes of untreated patients were similar to treated patients matched by similar disease characteristics. This study suggests that initial NTM is a viable option but only in the mildest cases, with watchful waiting after induction treatment.
Pediatric Inflammatory bowel disease: Initial experience from a single centre in North India

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Objectives and Study: Inflammatory bowel disease in children has only recently been described from India. The majority of literature for Paediatric IBD (PIBD) is from Europe and North America. India is at a unique cross roads. The region is rapidly developing socioeconomically and has the genetics for PIBD resulting an increasing diagnosis of this condition. Primary care physicians are also unaware that PIBD is an important differential diagnosis to be considered. In this setting the objective of this study was to describe our cohort of PIBD at a referral Paediatric centre in North India

Methods: The data records of patients upto 18 years of age diagnosed as Paediatric IBD (PIBD) who attended the Paediatric Gastroenterology clinic from September 2015 to March 2022 were reviewed. The patients were classified into Ulcerative colitis (UC), Crohn’s disease (CD) and Indeterminate colitis (IC) based on clinical, laboratory investigations, endocopy and histopathology. The treatment comprised of sulfasalazines, immunosupressants, biological agents, exclusive enteral nutrition (EEN) and Crohns disease Exclusion diet with Partial Enteral Nutrition (CDED + PEN). The response to therapy and relapses were recorded using PUCAI/PCDAI scoring.

Results: A total of 90 paediatric patients with 57% males (n=52) were diagnosed as PIBD. According to subtype classification, 54(60%) patients had Ulcerative Colitis , 30 patients (33.3%) had Crohn’s disease and 6 (6.7%) patients had Indeterminate Colitis. The median age at diagnosis was 12 years (range : 6m-18years) and median delay in diagnosis was 12 months (range: 1month-10 years). Patients with CD commonly presented with pain abdomen (n=28, 93.3%), weight loss (n=22, 73.3%) and growth failure (n=16,53.3%). 5 cases presented with occult Gastrointestinal bleed and isolated small bowel Crohns Diagnosed by Capsule endoscopy. UC cases presented with bloody stools (n=54, 100%), abdominal pain (n=38,70.3%). Extraintestinal manifestations were seen in 26(28.8%) patients. Stunting and wasting was present in 17.7% patients. Radiological abnormalities were present in 42% (n=38) cases. Induction therapy with mesalamine and steroids was given in 46 UC patients (81.4%), 26 CD patients (86%) and all IC patients. Azathioprine was given in 52 cases (57.7%) as maintenance therapy. Surgery was required in 3 cases (1 acute severe colitis with perforation, 1 diversion ileostomy in intractable CD, 1ileal stricture in CD). 15 patients received biologicals (Infliximab -14, Adalimumab -1). The median duration of follow up was 20 months (range : 2-72 months). Clinical remission was seen in 76% of UC patients (n=38) , 78.5% (n=22) CD patients and all IC patients. 20 patients (22.2%) were diagnosed as Very early onset IBD (<6 years of age) [UC=14,CD=2,IC=4]. The mean age at presentation was 36.9±13.6 months.). Exome sequencing was done in 10 patients (XIAP 1, IL10 defect 1). The child with IL 10 defect received a HMSCT.

Conclusions: We describe a cohort of PIBD from a tertiary referral centre in North India. UC was more common than CD and a significant number 22% were younger than 6 years at disease onset with 2 described monogenic defects. The number of cases seen has increased each year. Whether this is due to an increased recognition or an increased incidence of PIBD in this region remains to be seen.
Earnings in adult age in patients with childhood-onset inflammatory bowel disease: a nationwide population-based cohort study

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Objectives and Study: IBD with onset during childhood seems to represent a severe disease phenotype with increased morbidity. We have previously demonstrated that children with IBD have significantly lower final grades in compulsory school compared to healthy peers. There is, however, little information on the association of childhood-onset IBD with later professional career and subsequent earnings.

Methods: We identified 5,404 individuals diagnosed with childhood-onset IBD (<18 years) between 1990-2014 (ulcerative colitis: n=2,818, Crohn’s disease: n=2,328) in the Swedish National Patient Register. Patients were matched with 10 general population reference individuals by sex, birth year and place of residence (n=51,295). Data on earnings during 1992-2017 were obtained through the Longitudinal integration database for health insurance and labour market studies. Earnings were converted into Euro (inflation-adjusted to 2019). The differences in earnings between patients and general population reference individuals were calculated through quantile regression.

Results: Patients with childhood-onset IBD had significantly lower annual taxable earnings from age 20 through age 30 (adjusted median annual income difference (AMAID) at age 30: -5.4% (95% CI -9.1% to -1.8%)). Particularly lower annual taxable earnings through early adult age, were seen in patients that during childhood had been exposed to surgery or long-term inpatient IBD treatment (>30 days) (AMAID at age 30: -16.3% (95% CI -24.7% to -7.9%)).

Conclusions: Most patients with childhood-onset IBD have comparable earnings in early adult age as their healthy peers. However, the markedly larger, and by age increasing, absolute income gap in patients with more severe IBD during childhood, should be recognized.
Frequent occurrence of perianal disease and granuloma formation in patients with Crohn’s disease and concomitant orofacial granulomatosis 5 years after diagnosis

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Objectives and Study: Crohn’s disease (CD), can involve any part of the gastrointestinal tract and comprises a spectrum of phenotypes. Furthermore, extra-intestinal manifestations commonly accompany CD. One of these manifestations is orofacial granulomatosis (OFG), which is an inflammatory disorder of the perioral region and oral cavity that may appear as a separate disorder or in conjunction with various inflammatory systemic disorders, especially CD. CD in conjunction with OFG (CD-OFG), has been suggested to constitute a phenotype of CD with distinct features at diagnosis including frequent occurrence of perianal disease, however, there is a lack of longitudinal clinical data. The aim of this project was to study retrospectively a cohort of patients with CD-OFG, to evaluate whether the distinct phenotypic features persist in the years following the initial CD diagnosis.

Methods: Clinical data were extracted from medical records covering the first 5 years from diagnosis for 25 patients with CD-OFG (median age at diagnosis, 11 years; range, 4–23 years) and were compared with the corresponding data for 50 age- and sex-matched patients with CD without OFG (CD-Ref). The overall picture of CD including the presence of perianal disease was described for each patient using the Paris classification. Clinical characteristics, including perianal disease, presence of intestinal granulomas, and pharmacological and surgical treatments, were compared between the two diagnostic groups.

Results: Five years post-diagnosis, more patients with CD-OFG had perianal disease (64% vs 26%, P=0.002) and intestinal granulomas (88% vs 48%, P=0.0009) than the patients in the CD-Ref group (see Figure). They also more often had undergone perianal surgery (48% vs 8%, P=0.0002). Furthermore, among the patients with perianal disease in the CD-OFG group, 70% had undergone perianal surgery, as compared with 31% of the patients with perianal disease in the CD-Ref group (13/16 vs 4/13; P=0.03), indicating a more complex perianal involvement. At the end of the observation period, more of the patients with CD-OFG were receiving combination therapy, i.e., immuno-modulators (azathioprine or methotrexate) and tumour necrosis factor antagonists, than those in the CD-Ref group (36% vs 10%, P=0.01). Otherwise, no significant differences in the intestinal disease location and disease behaviour according to the Paris classification were observed between the two diagnostic groups 5 years after diagnosis.
Conclusions: Our results support the notion that CD in conjunction with OFG represents a distinct phenotype of CD which is characterised by a high risk of perianal disease and pronounced granuloma formation not only at the time of diagnosis but also persists over time post-diagnosis. Further, this patient group seems to have a need for extensive therapy, both in terms of surgical and medical treatment.
Disease course of ulcerative proctitis in children: a population based study on behalf of the SIGENP IBD Group.


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Objectives and Study: Ulcerative proctitis (UP) is a poorly investigated condition in children, usually considered as a minor form of Ulcerative Colitis (UC). The aims of the present study were to compare the disease course of pediatric patients affected by UP at diagnosis with the other UC locations and to possibly identify predictors of disease extension.

Methods: This multicenter retrospective observational study has been carried out starting from the data prospectively registered in the IBD Registry of the Italian Society of Pediatric Gastroenterology, Hepatology and Nutrition (SIGENP). Seventeen IBD referral centers adhering to the registry were included in the study. Patients age 0 to 18 years, who were diagnosed with UC according to the Porto criteria starting from January 1, 2009, to May 1st, 2021 were identified. Only children with a minimum follow-up of 12 months were included in the study. Once enrolled children were subsequently divided in two groups based on Paris classification: Group 1 (E1) and Group 2 (E2, E3 and E4).

Results: 872 children (median age at diagnosis: 11.2 years; range 1-17.4; M/F: 426/446) were included in the study. At diagnosis the following disease locations were identified: UP (E1) (9%, n=78); E2 (24%, n=210); E3 (13.3%, n=116); and E4 (53.7%, n=468). The median follow-up of enrolled children was 4.6 years (1-14.8). At the last follow up 702 (80.5%) children had at least one endoscopic re-evaluation. Excluding children with E4 location at diagnosis, we found that 28 out of 59 (47.5%) patients with UP showed a disease extension during the follow up versus 104 of 266 (39.1%) E2-E3 children, without significant statistical difference (p=0.2). Median time of the endoscopic extension was not significantly different between the two groups [(1.4 (0.4-6.4) years in the UP (E1) group vs 1.5 (0-10) years in E2-E3-E4 group; (p=0.8)]. Kaplan–Meier methods demonstrated cumulative probabilities of disease extension at 1, 5 and 10 years of 20.3% (95% CI 6-41.1%), 52.7% (95% CI 37.3-66%) and 72.4% (95% CI 52.2-85%) in the UP group (E1) and 14.6% (95% CI 7.2-24.5%), 35% (95% CI 27-43%) and 59.4% (95% CI 47.7-69.3%) in the E2–E3 group, respectively (log rank test p=0.07). When comparing UP group versus E2, E3, E4 group we did not find any statistical difference in the overall use of conventional immunsuppressants [19/78 (24.3%) vs 219/794 (24.3%), respectively; p=0.7] or biologic therapy during the follow-up [10 (13.9%) in the UP (E1) group vs 158 (20.6%) in E2-E3-E4 group, p=0.2]. The risk for colectomy was not different between the 2 groups [2 (2.8%) in the UP (E1) group vs 64 (8.6%) in E2-E3-E4 group, p=0.1]. Children with UP showing disease extension had increased median PUCAI [35 (10-80) versus 20 (10-45); (p<0.001)] and median ESR [24 (2-51) versus 8.5 (1-55); (p=0.04)] at diagnosis when compared with those without disease extension.

Conclusions: UP is a frequent location of pediatric onset UC and the risk of endoscopic extension of proctitis is similar to the more extensive forms. A considerable number of patients with UP required immunosuppressive or biologic therapy during the follow-up and no significant difference was observed in terms of surgery. Overall, UP cannot be considered as a minor form of UC. A higher PUCAI at diagnosis was found to be a relevant risk factor for disease extension of UP.
Intestinal ultrasound role in the management of pediatric inflammatory bowel disease: A prospective longitudinal cohort study

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Objectives and Study: Intestinal ultrasound (IUS) is an objective, non-invasive, cost-efficient tool for diagnosis and assessment of intestinal inflammation. Paediatric gastroenterologists are increasingly using IUS in clinical practice. Our aim was to assess the predictive value of IUS in children with inflammatory bowel disease (IBD).

Methods: A prospective longitudinal cohort study at the Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children's Hospital between 2015 to 2020. Participants were children (1-18 years) with a diagnosis of IBD. Patients were enrolled at any time during therapy or after a new diagnosis of IBD. Baseline IUS was performed at enrollment and every 3 months during regular visit for a total period of 2 years. We aim to assess the changes in bowel wall thickness by IUS, during 2-year follow-up.

Results: A total of 46 patients (19 females; 41%), with median age of 10 years (IQR 7.5-12), mostly with Crohn's disease (38/46) were included. A total of 223 IUS were performed during the study period. The median (IQR) terminal ileum wall thickness (Ti-WT) at baseline was 2.2 (2-3.5) mm. The outcomes of normalization of Ti-WT (<3mm) during therapy was achieved in 16/19 patients (84.2%) with Crohn's disease in a median time of 4 (IQR 3-7.5) months. Normalization of Ti-WT was associated with reduction of disease activity index and C-reactive protein response.

Conclusions: Sonographic measures of bowel wall thickness, have a potentially important role to play in the care of IBD patients as prognostic measure for disease outcome.
Effect of the Crohn's disease exclusion diet (CDED) on the fecal calprotectin level in children with active Crohn's disease.

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Objectives and Study: The CDED + PEN (partial enteral nutrition) is a promising method of nutritional treatment in active Crohn's disease (CD). An increase of fecal calprotectin (FCP) level - a marker of mucosal inflammation – happens to be the first evidence of the Crohn's disease exacerbation, ahead of clinical symptoms, and usually accompanies clinical symptoms. In this study we present our own experience with using the CDED + PEN in treatment of children with CD and higher FCP level.

Methods: Forty eight children (male/female: 27/21) in age 4-17 years (median value = 13.43; IQR=4.00) were treated with CDED + PEN between June 2019 and July 2021. The main inclusion criteria to the study was active CD defined as FCP level ≥ 250 µg/g. Patients with severe clinical manifestation of CD (PCDAI >40) or who started any new concomitant CD’s treatment later than at least 4 weeks before the start of dietary intervention were excluded from the analysis. The PCDAI and fecal calprotectin level were assessed at week 0 and 12. The primary endpoint was ITT normalization of FCP level that is result< 250 µg/g at week 12. Wilcoxon Matched Pairs Test was used for statistical analysis.

Results: The normalization of FCP level was obtained in 35 % (17) of children and the minimum 50% decrease of FCP level in 54% (26). The reduction of fecal calprotectin level between week 0 and week 12 was statistically significant with median value = 1045 µg/g; IQR=1188 and 363 µg/g; IQR=665, respectively (p<0.05). Among 29 patients who were not in clinical remission at baseline 16 (55%) obtained clinical remission (PCDAI<10) at week 12 and 20 (69%) clinical response defined as a drop in PCDAI of at least 12.5 points or remission. In this group the reduction of PCDAI between baseline and week 12 was statistically significant (median value = 20 points; IQR=7.5 and 5.0 points; IQR=5.0, respectively (p<0.05)). All patients with normal FCP level at week 12 were in clinical remission. In 10 children (21%) the full course of 12 weeks with CDED+PEN was not completed or the concomitant therapy had been started before week 12 due to the lack of efficacy/intolerance of nutritional treatment.

Conclusions: The 12-weeks course of treatment with the CDED + PEN has a beneficial effect on the fecal calprotectin level in children with active CD. Dietary intervention leaded to significant decrease in the FCP level in studied group and to the normalization of this parameter in every third patient.

Conflict of Interest: industry sponsored presentations (by Nestle)
P-091

Change of subtype and progression of childhood-onset inflammatory bowel disease.

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Objectives and Study: Childhood-onset inflammatory bowel disease (IBD) is often described as more aggressive disease and with more rapidly increasing extension and complications over time than adult-onset IBD. Frequency estimates of subtype changes and phenotype progression in PIBD have however varied in the literature (15-20% and 15-39% respectively), partly because of the different types of study populations (mostly referral centers) used. We therefore aimed to study the change of subtypes and phenotype progress of childhood-onset IBD during childhood, using recently updated subtype definitions in an era of modern treatment.

Methods: We identified a random sample of 233 individuals of all 4963 patients diagnosed with PIBD in the National Patient Register between 2002-2014. Of those, 147 patients underwent endoscopies before referral to adult care, which made it possible to reevaluate subtype and phenotype using the Porto and Paris classifications. All medical notes were reviewed and proportion of children who changed subtype (according to the smartphone app IBD classes) and whose phenotype progressed during childhood were reported.

Results: Figure 1. Change in subtype, extent, location, and behaviour in childhood-onset inflammatory bowel disease patients between time of first IBD diagnosis and referral to adult care.
Median follow-up was 64 months (95%CI 39-87). Only 8/147 (5%) patients changed subtype during follow-up, of which none from Crohn disease (CD, Figure 1). As expected, at diagnosis the majority of ulcerative colitis (UC) patients had pancolitis (50/72, 69%) and ileocolonic involvement was the most common presentation of Crohn’s disease (25/65, 38%). Only 3/72 (4%) patients with UC increased extent during follow-up. Location progressed in 6/65 (9%) patients with CD during follow-up. Of the 5/70 (7%) patients who changed disease behaviour during childhood, four patients with inflammatory behaviour progressed to strictures and one patient to penetrating disease.

**Conclusions:** During childhood, patients with childhood-onset IBD rarely changed subtype and few patients experienced progression of extent in UC or location/behaviour in CD.
Objectives and Study: While acute pancreatitis is a well-known complication in about 3% of adults who use thiopurines for inflammatory bowel disease (IBD), this phenomenon is less well documented in children. We aim to explore thiopurine-induced pancreatitis in a cohort of children with IBD at a tertiary UK centre, with specific objectives to determine:

- The time of onset and outcome of acute pancreatitis.
- If thiopurine-induced pancreatitis represents an absolute contraindication to the use of an alternative thiopurine.
- If there is a correlation between thiopurine induced pancreatitis and concomitant thiopurine metabolite levels.

Methods: A list of children under 18 years with raised lipase over a 5-year period from January 2017 to March 2022 was obtained from the hospital laboratory. Children were selected if they had an underlying diagnosis of IBD, and had developed pancreatitis following commencement of a thiopurine medication (Azathioprine and 6 Mercaptopurine). Acute pancreatitis was defined as a lipase level twice above the upper limit of normal, in addition to clinical signs typical of pancreatitis.

In considering the relationship between thiopurine metabolite levels and the onset of acute pancreatitis, 6-Thioguanine Nucleotide (6-TGN) levels were considered relevant if measured within 2 weeks either side of the onset of pancreatitis. Levels were categorised as low (<230pmol/8.108 RBC), normal (230-450pmol/8.108 RBC) and high (>450pmol/8.108 RBC).

Results: 16 patients, predominantly male (12) were identified with thiopurine-induced pancreatitis during the time period studied. The mean age at diagnosis of IBD was 11.6 years. The median time to starting Azathioprine from diagnosis of IBD was 4 months and the mean dose of Azathioprine was 1.7mg/kg and 6-MP 0.8mg/kg. 15/16 patients had a documented normal TPMT activity prior to commencing thiopurines and one had a low level. 4 of the 16 patients already had elevated pancreatic enzymes as part of the IBD presentation prior to starting Azathioprine.

The median time point of presentation with symptoms of pancreatitis was 38.5 days (range 5 days to 3 months) days. This resulted in the medication being withheld in all 16 patients and complete resolution of pancreatitis.

Following resolution of pancreatitis, thiopurines were reintroduced in 9 patients (4 on Azathioprine and 5 on 6MP). Pancreatitis reoccurred in 3 (1 patient on Azathioprine and 2 patients on 6-MP) within a week of restarting (2-4 days) resulting in withdrawal of the medication and followed by complete resolution of pancreatitis. The remaining 7/9 patients who recommenced thiopurines have continued without recurrence of pancreatitis.

6/15 patients had a documented 6-Thioguanine Nucleotide (6TGN) levels thiopurine metabolite level available within 2 weeks of the onset of pancreatitis. 1 had a high level, 3 had low levels and 2 had levels within a normal range.

Conclusions:

- Thiopurine-induced pancreatitis is an idiosyncratic side effect that is unlikely to occur beyond the first three months following commencement with Azathioprine/ 6 MP.
- Following resolution of thiopurine induced pancreatitis, recurrence of pancreatitis occurs in 30% of children with IBD who re-start thiopurines.
- The need for long term immunosuppression in PIBD patients may justify the cautious re-introduction of thiopurine medication in children who recover from thiopurine induced pancreatitis.
Analysis of the actual use of enteral nutrition therapy for childhood-onset Crohn’s disease using the Japanese Paediatric Inflammatory Bowel Disease Registry: final report.


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Objectives and Study: The Japanese Paediatric Inflammatory Bowel Disease Registry is a web-based, prospective, multicentre study aimed at clarifying the characteristics and natural history of patients with children with IBD in Japan. Using data from the registry, we investigated the actual use of enteral nutrition (EN) and the effect of maintenance treatment.

Methods: Of the 262 patients with childhood-onset Crohn’s disease enrolled from participating institutions between October 2012 to March 2021, 146 who were followed for 1 year or more were analyzed (participating institutions: 16 centres, median age of onset: 12.5 years, median observation period: 4 years).

Results: In total, 142/146 (97%) were on EN during the study period. All but one case were treated with elemental formula. Sixty-eight of 146 (47%) were treated with EN ± mesalazine (EN monotherapy). Thirty-six (53%), and 25 (37%) of those 68 patients remained on EN monotherapy at 6-months and 1-year follow-up, respectively. Twelve patients (18 %) in the EN therapy group were followed up without any additional therapy during the disease (median observation period: 3.5 years). EN was also used as maintenance therapy for patients who induced remission with steroids or biologics. Twenty-eight of 146 (19%) started treatment with a combination of EN and steroids. Three patients who were able to wean off steroids were subsequently maintained with EN monotherapy (median observation period: 5.5 years). To evaluate the change in second-line therapy over the period, we divided fifty-six patients who were difficult to be kept in remission with EN monotherapy into two groups by the registry year (first group: 2012–2015, second group: 2016-2021). The first group consisted of 29 patients, with the breakdown of secondary treatment 18 (62%) on biologics, 9 (31%) on steroids, and 12 (41%) on IM. The second group consisted of 27 patients, 19 (70%) on biologics with the breakdown of secondary treatment, 4 (15%) on steroids, and 7 (26%) on IM. The two groups had no significant differences (p=0.34).

Conclusions: Approximately one-third of the patients in the EN monotherapy group were treated successfully without additional therapy, such as immunomodulators, during the first year of treatment. EN can be recommended for all childhood-onset Crohn’s disease considering its high safety profile regardless of the clinical features.
P-094 (Poster of distinction)

Adolescents and young adults with IBD controlled by the STRIDE-II strategies had poor HRQL in school and work domains rather than physical impairment

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Objectives and Study: Inflammatory bowel diseases (IBD), encompassing Crohn’s disease (CD) and ulcerative colitis (UC), are chronic and disabling disorders, that often have their onset among adolescents and young adults (AYA). IBD are characterized by episodes of active disease interspersed with remission and its activity is inversely correlated with health-related quality of life (HRQL) and cause disabilities. The STRIDE-II strategies ("treat-to-target") to control the disease confirmed that clinical remission, endoscopic healing, restoration of HRQL, and absence of disabilities are one of the most important long-term achievable treatment targets for patients with IBD. Abdominal pain is one of the most common disabling problem in IBD patient and may occur as an associated symptom of inflammation in the GI tract, sequelae of procedure or a side effect of treatment.

This study aimed to determine whether AYA with IBD in clinical remission or with low disease activity using the "treat-to-target" strategies would exhibit HRQL and pain disability similar to that of age-matched healthy individuals, by using a ‘patient-reported outcome’ (PRO) instruments and visual analogue scale (VAS) for pain.

Methods: This study enrolled AYA with IBD, from five multidisciplinary clinics. All patients selected was in remission or had a long term low disease activity using the "treat-to-target" strategies. A total of 59 AYA with IBD (age, 13–25 years) and 60 healthy AYA (age, 13–25 years) completed the HRQL questionnaires according to the age: the Paediatric Quality of Life Inventory 4.0 (PedsQL™4.0) the 36-Item Short-Form Health Survey questionnaires and the VAS for pain: FACES pain rating scale, and total VAS scores for pain. Demographic data, extra-intestinal manifestations, treatment, and outcomes regarding CD and UC were evaluated.

Results: AYA with IBD and healthy controls were similar with respect to median ages (18.63 [13.14–25.80] years vs 20.5 [13.68–25.84] years, $P=0.598$), proportion of female sex (42% vs 38%, $P=0.654$), and percentage of upper middle/middle socioeconomic classes (94% vs 97%, $P=0.596$). The PedsQL™4.0school/work domain score was significantly lower in AYA with IBD than in healthy controls (70 [10–100] vs 75 [5–100], $P=0.037$). The SF-36 ‘general health-perception’ score was significantly lower in AYA with IBD than in healthy controls (50 [10–80] vs 0 [25–90], $P=0.0002$). The median VAS pain, FACES pain rating scale, and total VAS pain scores were similar between the two groups (2 [0–10] vs 3 [0–9], $P=0.214$). No association between HRQL and clinical and demographic parameters was identified among CD and UC patients.

Conclusions: This study showed that AYA with IBD and controlled a long term by the "treat-to-target" strategies did not reach a normalized HRQL, but had no pain disability. The low school/work domains and general health perception highlighted others disabilities criterion in this vulnerable population.
P-095

Analysis of the serologic response to COVID-19 Vaccination in pediatric Inflammatory Bowel Disease

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Objectives and Study: Paediatric Inflammatory Bowel Disease (pIBD) is a chronic disease that often requires immunosuppressive drugs such as glucocorticoids, thiopurines or biologic therapy, which may attenuate the response to certain vaccines. The SARS-CoV2 pandemic in 2020 prompted the rapid development of multiple vaccines and, although there are not many studies regarding their response in patients with IBD, it seems that there are differences in adults patients in relation to the treatment they receive. To the best of our knowledge, there is no literature on paediatric patients with IBD. The aim of the present study is to assess the response to COVID-19 vaccination in pIBD patients.

Methods: In July 2021, vaccination against COVID 19 was authorised for adolescent patients from 12 years old. A prospective study was conducted in a tertiary hospital from July to December 2021 including pIBD patients from 12 to 18 years of age who agreed to be vaccinated. We determined baseline COVID-19 serostatus and analysed the serologic response after the complete vaccination regimen: 1 dose (patients with previous COVID-19 infection) or 2 doses (those with no previous infection) of mRNA vaccine. During this period, three different immunoassay tests have been used for the semi-quantitative and qualitative determination of IgG antibodies against SARS-CoV2, which use different units of measurement and are not comparable with each other. We recorded clinical and epidemiological data. Statistical analysis was performed using SPSS® software.

Results: We included a total of 33 patients, 19 (56%) were male. The median age was 14.85 years (age range from 12 to 17.7). A total of 26 (79%) were diagnosed with Crohn’s Disease, five (15%) with Ulcerative Colitis and two (6%) with unclassified IBD. Up to 23 patients (70%) were receiving biologic treatment and 20 (61%) had immunosuppressive treatment. Eight participants (24%) have undergone a COVID-19 infection, and in all cases reported mild or non-existent symptoms: seven of them (88%) were infected before the vaccination and only one (12%) after it. A total of 32 patients (97%) received the BioNTech/Pfizer® vaccine (COMIRNATY) and one received MODERNA®. Only five participants (15%) reported side effects after the vaccination, and these were in all cases mild (myalgia, headache, and low-grade fever, lasting less than 24 hours). Both the baseline and the post-vaccination serologic status were determined in 22 patients, and in seven patients only the post-vaccination status was carried out. All of them showed an adequate serologic response after the complete vaccination regimen. The development of adverse effects was independent of having suffered COVID-19 (p=0.17) and independent of treatment (p=0.12). We found no statistical differences between patients receiving thiopurines or biologic treatment versus those without this kind of treatment (p=0.253 and p=0.521 respectively).

Conclusions: The present preliminary study suggests that the pIBD population show an adequate response to the recommended vaccination regimen and the approved vaccines seem to be safe in this group of patients. Receiving thiopurines or biologic treatment did not seem to influence the serologic response. However, the small number of patients and the impossibility to compare antibody levels with different tests, limits the drawing of conclusions.
**P-096**

**Video capsule endoscopy in pediatric inflammatory bowel disease: indications, findings and other related outcomes**


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**Objectives and Study:** Video Capsule Endoscopy (VCE) is a noninvasive imaging technique that allows mucosal visualization and has been demonstrated to be useful in the diagnosis and follow-up of adult patients with Inflammatory Bowel Disease (IBD). However, its clinical implications and applications in the pediatric population are still poorly studied. The aim was to review the indications for VCE in pediatric patients with suspected or confirmed IBD, to analyze the therapeutic implications of its results and to explore the potential impact of the establishment of the Porto criteria.

**Methods:** We performed a descriptive and retrospective single-center study with a cohort of patients under 18 years of age who underwent VCE due to suspected or confirmed IBD in a tertiary hospital from February 2007 to January 2022. Demographic, anthropometric, clinical, and analytical data were collected. The study was considered complete in those in which the arrival of the VCE in the cecum was observed. The statistical study was performed using SPSSv.28 software.

**Results:** A total of 40 patients were included. The mean age at the time of the test was 10.5±4.4 years and 52% (21) were male. The indications for the VCE were gastrointestinal bleeding in 4 (10%) patients, suspected IBD for other reasons in 5 (12.5%), follow-up of IBD in 23 (57.5%) and IBD extension study at diagnosis in 8 (20%). A total of 31 (77.5%) patients had Crohn's disease (CD), 6 (15%) ulcerative colitis (UC) and 3 (7.5%) unclassified IBD.

Most of the children (95%) underwent a liquid diet for bowel preparation the day before the VCE and the study was complete in 30 (75%) of the cases. We observed a higher proportion of complete studies in children who received a liquid diet in comparison to those who took laxatives or a combination of laxatives and liquid diet although this difference was not statistically significant (p=0.052). In 21 patients (52%) the VCE was swallowed voluntarily, with statistically significant differences according to age: oral ingestion was performed mainly in older children (13.34±3.18 years), while placement by Upper Gastrointestinal Endoscopy (UGE) was more frequent in the youngest (7±2.87 years) (p<0.001). In 11 patients (27%) the Patency capsule was previously administered, and VCE was contraindicated in 2 (5%) due to delayed expulsion and/or deformation of the capsule. Complications were observed in 4 (10%) of the patients, consisting of self-limited bleeding related to placement by UGE in 2, and VCE retention in another 2. We found no age-related differences.

In 8 (20%) of the children, the VCE results implied a changed of the diagnosis. After the modification of the Porto Criteria in 2014, the pediatric IBD-related indications for VCE went from 8.9% to 38.9% of the total in our center (p<0.01).

**Conclusions:** In our center, VCE placement by UGE was significantly more frequent in the younger patients. Also, those who received an exclusively liquid diet the day before the VCE were more likely to have a complete exploration. In addition, VCE has an impact on the diagnosis and therapeutic approach of pediatric IBD patients. Although the rate of complications is higher than that described in adults, VCE can be considered a safe and non-invasive technique with a promising future in the management of these patients.
Multi-linguistic validation of the IMPACT-III instrument to assess the quality of life of Indian children with inflammatory bowel disease

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Objectives and Study: Quality of life instruments have not been validated for Indian children with inflammatory bowel disease (IBD). We aimed to validate the most widely used disease specific quality of life instrument for paediatric IBD patients in 3 Indian languages – Hindi, Tamil and Bengali, in 6 centres across India.

Methods: 102 paediatric IBD patients under follow up in 6 centres across India were enrolled. IBD disease activity scores were individually calculated and disease severity was classified as remission, mild, moderate or severe disease. Each parent-child dyad was given 3 questionnaires. The IMPACT-III and Paediatric Quality of Life Inventory, Version 4.0 (PedsQL™), child questionnaire were administered to the children, while the PedsQL™ parent questionnaire was completed by the parent. Principal factor analysis was used to determine the optimal domain structure for our study population. Internal reliability testing was done by analysing the Cronbach's alpha, ANOVA test was applied to determine discriminant validity and concurrent validity was worked up by assessing the correlation between IMPACT-III & PedsQL™ using Spearman's correlation coefficients.

Results: The IMPACT-III questionnaire with its original 4 domain structure was not appropriate for our study population. For all the three languages analysed, the most suitable solution was a five-domain structure: Concerns, Social Acceptance, Mental Disposition, Disease Adjustment & Self-confidence, all of which demonstrated good internal reliability (α=0.73-0.93). However, three questions had to be dropped to attain this reliability. Discriminant validity was also significant (p < 0.001) between the IMPACT-III scores and the IBD disease activity scores. The concurrent validity between IMPACT-III and PedsQL™patient questionnaires and IMPACT-III and PedsQL™parent questionnaires also showed significant correlation (p <0.001 to 0.024).

Conclusions: The IMPACT-III questionnaire in its Hindi, Tamil and Bengali versions demonstrated good validity and reliability for Indian population, although our findings suggest a different domain structure than originally proposed.
Modification of anthropometric parameters and body composition during anti-TNFα treatment in paediatric inflammatory bowel disease


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Objectives and Study: Children and adolescents with inflammatory bowel disease (IBD) have altered body composition (reduced fat free mass -FFM- and body mass index-BMI) at diagnosis compared to healthy controls. In addition, treatment with anti-TNFα drugs is associated with body weight gain primarily caused by an increase in fat mass (FM). Overweight and excess adiposity are known to be risk factors for metabolic and cardiovascular diseases but also for loss of response (LOR) to anti-TNFα. Aim of our study is to prospectively evaluate modification of anthropometric parameters (body weight, BMI) and body composition (FM%, FFM%, total body water) in pediatric IBD patients, during treatment with anti-TNFα drugs.

Methods: Thirty anti-TNFα naïve IBD children (age 6-18 years) were consecutively enrolled from January 2020 to May 2022. Every patient underwent a complete nutritional evaluation including measurement of anthropometric parameters, body composition (fat mass- FM%, FFM%, total body water-TBW%) with bioelectrical impedance analysis (BIA) and serum metabolic analysis (glycemia, insulin, total cholesterol, HDL, LDL, tryglicerids). All these tests were performed at baseline (initiation of anti-TNFα treatment), at 3, 6, 12 and 24 months of treatment.

Results: A total of 17 patients completed follow up at 12 months. Two patients presented LOS and were excluded from the study, also subjects with concomitant treatment with steroids were excluded. The majority of patients had Crohn’s Disease (CD 16/17, 94%), only 1 patient had unclassified IBD (1/17, 6%). Partial enteral nutrition (PEN) with polymeric formula was used in 8/17 (47%), and only 1 patient received a CD specific diet. From baseline to 12 months of treatment, we observed an increase of weight z-score (-1.09 ± 1.12 vs 0.13 ± 0.4, p=0.06), as well as an increase of BMI (-0.79 ± 1.3 vs 0.8 ± 0.5, p=0.02) and FM% (19.9 ± 5.02 vs 28.2 ± 6.5, p=0.04). FFM% (76.8 ± 9.69 vs 67.4 ± 5.3, p=0.11) and total body water (TBW% 58.78 ± 3.36 vs 54.35 ± 3.7, p=0.10) reduced from baseline to 12 months. No statistically significant difference was found in terms of glycemia, insulin, total cholesterol, HDL, LDL, and tryglicerid levels.

Conclusions: In our prospective study we observed a statistically significant increase of body weight, BMI and FM in IBD children and adolescents after 12 months of treatment with anti-TNFα drugs. This effect could be caused by progressive mucosal healing, amelioration of nutrient absorption and increased appetite, but also by increased adipogenesis due to a direct effect of anti-TNFα on metabolism. Nutritional monitoring and follow-up is important in order to early diagnose overweight and identify patients at higher risk of metabolic disease and eventually secondary LOS to ongoing treatment.
What do young people with inflammatory bowel disease, their parents/carers and clinicians value for inclusion in a disease-specific electronic medical record?


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Objectives and Study: ‘CCCare’, an existing inflammatory bowel disease (IBD)-specific electronic medical record, is being upgraded to include paediatric functionality (CCCare-P). CCCare-P aims to enhance quality of care and optimise transition. During design, clinicians determined functionalities considered important for inclusion via a “Consensus Process”1. As consumer co-design is vital to successful complex care, young people with IBD and their parents/carers were then also consulted on topics they felt should be included. Here, we report on patients’ and parents'/carers’ views as compared with clinicians’.

Methods: Online surveys were advertised via email and social media of Australian and New Zealand consumer groups (CCA & CCNZ) for 3 months (Sep-Dec 2021). Young people with IBD (<18 years) and parents/carers provided online consent and demographic data. Participants were shown a descriptive list of software inclusion topics as previously agreed by clinicians. They were asked to indicate their opinion as to whether each topic should be included by selecting the responses yes, maybe or no. Participants were able to provide comments and also suggest other topics for inclusion. Descriptive statistics were used. The study had ethics approval and was funded by The Leona M. and Harry B. Helmsley Charitable Trust.

Results: There were a total of 151 respondents. Of the 32 young people, 56% were male, 66% had Crohn’s disease (CD), 63% were diagnosed 1-5 years ago and 12% reported intestinal surgery. The greatest proportion of young people were in the “8-12 Years” age group (38%). Almost half (47%) were treated with “tablets, capsules, sachets or suppositories/enemas” only, and 72% rated their IBD control as ≥6 on a 1-10 scale (1=worst it’s ever been, 10=best). Of the 119 parent/carer respondents, 91% were female. Most (62%) were aged 41-50 years and their children were almost equally split in gender (male=55%). Most parents/carers had children in the “13-15 Years” age group (44%) and 73% had children with CD.

Across the three groups, there was general agreement (>70%) to include Quality of Life, Mental Health, Self-Management Tasks and Transition Readiness (figure 1). Greater differences were seen across groups in the General IBD Facts, Your IBD History and Satisfaction topics. Cost saw the greatest disparity, being less supported by young people and their parents/carers (<50%) compared to clinicians (76%).

Additional topics suggested for inclusion by young people included Pain Measurement and Diet/Nutrition. The latter was also suggested by parents/carers, in addition to Access to Care and Social Relationships. 84% of young people and 87% of parents/carers supported the idea of online pre-consultation completion of clinical assessments via CCCare-P.
Figure 1 – Support for Topics in Clinician, Young People and Parent/Carer Groups

Conclusions: While general support across all three groups was noted for half the suggested topics, significant differences in opinion were present. This elucidates the importance of widespread consumer consultation in highlighting differing perspectives. Of note, all topics with a >70% “yes” vote in any group were implemented into CCCare-P, ensuring it is fit-for-purpose to all, thus maximising future engagement.


Conflict of Interest: Susan Connor: received honoraria for Advisory Board participation, speaker fees, educational support and/or research support from: Abbvie, BMS, Celltrion, Chiesi, Eli-Lilly, DrFalk, Ferring, Fresenius Kabi, Gilead, GSK, Janssen, MSD, Novartis, Organon, Pfizer, Sandoz, Takeda, Agency for Clinical Innovation, Gastroenterological Society of Australia, Medical Research Future Fund and The Leona M and Harry B Helmsley Charitable Trust.


Richard Gearry: research support, advisory board and educational activity to AbbVie, Janssen and Zespri. Also on advisory board for Celltrion and part of educational activities for Takeda and Pharmac.
Prevalence, management and outcome of mycobacterium tuberculosis infections in paediatric patients with inflammatory bowel disease in Singapore: A 13-year review

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Objectives and Study: Mycobacterium tuberculosis (TB) infection is more prevalent in Asian populations compared to Western countries and can pose diagnostic and management challenges in patients with chronic inflammatory bowel disease (IBD). Increased risk of TB reactivation has also been associated with anti-tumour necrosis factor (TNF) therapy. The aim of the study is to examine the prevalence, characteristics and treatment outcomes of TB infection in a Southeast Asian cohort of paediatric IBD patients at a single centre in Singapore.

Methods: Retrospective review of paediatric patients (0-18 years) diagnosed with IBD from 2008-2021 was performed at a single tertiary unit, and patients who received treatment for TB were identified. TB screening was based on interferon-gamma releasing assay (IGRA), tuberculin skin test (TST) and/or chest radiograph in addition to clinical history and was performed prior to initiation of anti-TNF therapy. Since 2013, earlier TB screening has been performed at the time of IBD diagnosis prior to any immunosuppression. Diagnoses of latent TB infection and active TB disease were based on criteria defined by Centers for Disease Control and Prevention (CDC).

Results: TB infection was detected in 12 out of a total of 256 IBD patients (prevalence 4.6%). 10 patients had Crohn’s disease and 2 had ulcerative colitis. Anti-TNF therapy was used in 5 patients. Median age at diagnosis of IBD was 11 years (range: 1-17). TB was diagnosed based on IGRA (n=9), TST (n=2) and clinical/histopathologic findings (n=1). 9 patients had latent TB, of whom 7 were detected prior to starting any immunosuppressive treatment, 1 while on methotrexate and 1 while on anti-TNF. Of the 3 patients with active TB, 1 was diagnosed prior to IBD treatment, while 2 had de novo active TB disease while on anti-TNF (n=1) and azathioprine (n=1) and were screened negative for TB prior to treatment. The incidence rate of active TB disease with immunosuppressive therapy in our cohort was 0.3 per 100 patient-years. Treatment for latent TB consisted of isoniazid monotherapy for 9 months (n=4) or combination therapy with isoniazid, rifampicin, pyrazinamide and/or ethambutol for 6-9 months (n=5). For active TB disease (n=3), treatment comprised of isoniazid/rifampicin/ethambutol/pyrazinamide for 2 months followed by isoniazid/rifampicin for 4 months. Immunosuppressive therapy was interrupted or delayed by a median interval of 2 months (range: 0.01-28) from initiation of TB treatment. After a median follow-up duration of 7 years (range: 2-13) none of the 12 patients had active or reactivated TB infection or serious adverse events with anti-TB medication. At last follow-up, all 12 patients had not achieved remission of their IBD; median faecal calprotectin level was 383 µg/g (range: 39 - >1000).

Conclusions: Latent and active TB infections affect a significant proportion of children with IBD in our Southeast Asian cohort. Expanding TB screening to all IBD patients at the time of diagnosis and close TB surveillance while on immunosuppressive treatment may lead to earlier identification and treatment of patients at-risk.
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Impact of induction therapies on anthropometric indices in luminal Crohn's disease


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Objectives and Study:

1. To assess whether there is an impact of EEN as primary induction therapy on anthropometric parameters in children with inflammatory Crohn's disease in secure remission at one year post diagnosis.
2. To evaluate the impact of different induction therapies on anthropometric indices at one year.

Methods: A retrospective review of records for all Crohn's disease (CD) patients diagnosed between January 2020 and December 2020 was done. Patients with stricturing/penetrating phenotype or those requiring surgery were excluded from analysis. We used clinic notes, letters, investigations to collect our data.

Results: 29 children were diagnosed with inflammatory CD of which 20(66.6%) were males and 9(31%) were females. The average age at presentation was 13.3 years. 20(66.6%) patients received exclusive enteral nutrition (EEN) at presentation, 1 received partial enteral nutrition and 8 received other treatments(steroids/biologics). 9(31%) needed biologics as top down therapy, 7(24%) were started on azathioprine. All patients were in secure clinical (patient reported outcomes and clinical assessment) and biochemical remission (CRP, ESR and fecal calprotectin) at the end of one year. Maintenance therapy for patients included azathioprine, biologics. Paired t test revealed significant improvement in weight z-score(p<0.000) for all treatment groups at one year, however did not show a significant improvement in height z-score (p0.6). There was no significant difference between improvement in weight or height z-scores when EEN was compared with other induction therapies (p values 0.4 for weight and 0.15 for height).

Conclusions: EEN is an established therapy for luminal Crohn's disease with growth failure. Whilst, EEN did improve weight z-scores, height z-scores did not seem to improve significantly at one year. Other induction agents were equally efficacious as EEN in improving weight z-scores at one year. Further longitudinal follow up may be needed to establish improvement in height z-scores over time.
Large Vessel Vasculitis as extraintestinal manifestation (EIM) of Inflammatory Bowel Disease (IBD)

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Objectives and Study: Extraintestinal manifestations (EIM) are relatively common in pediatric patients with inflammatory bowel disease (IBD). We describe a rare extraintestinal complication of large vessel vasculitis (LVV - Takayasu’s arteritis) in 16-year-old young man. There is only sparse literature LVV in patients with IBD and treatment is challenging.

Methods: A retrospective review of clinical notes and investigations was undertaken with review of literature. Only 29 cases of CD with Takayasus have so far been reported in adolescents. The chances of both existing in the same patient is 1 in 10 million.

Results: A 16-year-old young man of Eastern European descent was diagnosed at 2 years of age with very early onset IBD, managed as Ulcerative colitis. Initial treatment comprised Sulfasalazine and Azathioprine with frequent relapses responsive to steroids. Treatment was escalated to Infliximab (combination therapy with Azathioprine) following an endoscopy which showed pancolitis at 13 years of age. He lost immunologic response to Infliximab and was switched to Adalimumab to which he also experienced secondary treatment failure.

Symptoms persisted with abdominal pain, bloody stools, nocturnal symptoms. Endoscopic assessment was suggestive of Crohn’s disease with ulcerations in duodenum, jejunum, terminal ileum (deep seated) with patchy involvement of colon with histological evidence only limited to active pancolitis. MRI small bowel showed thickening of terminal ileum. He continued to be steroid dependent. Serum inflammatory markers were persistently elevated along with raised faecal calprotectin: Erythrocyte sedimentation rate > 60mm/hr, CRP >70mg/L, Platelets >500x 10^9/L and IgA elevated >2.9g/L. Extensive immunological work up (anticardiolipin antibodies, angiotensin converting enzyme, rheumatoid factor, anti dsDNA antibodies, complement and antinuclear antibodies) was negative.

Treatment was escalated to Vedolizumab with improvement in bowel symptoms, but inflammatory markers remained persistently elevated and he complained of pain in left mandibular region. Carotid ultrasound suggested stenotic disease of the carotid arteries and a widespread large vessel arteritis (LVV) involving the aorta, subclavian, carotids was confirmed on PET scan with a mixed picture of damage and active inflammation.

Since LVV is life-threatening, high dose, pulsed intravenous steroids were started, vedolizumab stopped and Tocilizumab (treatment of choice for LVV) started with joint rheumatology management. Aspirin and methotrexate were also added. His arteritis was controlled on this regimen but continued to have gut symptoms along with perianal disease. He had two setons inserted which allowed to heal his perianal disease but eventually had a subtotal Colectomy with ileostomy formation.

Conclusions: Although rare, IBD patients are at a risk of LVV. We need to have high index of suspicion where IBD patients with significantly raised inflammatory markers or unusual symptoms to screen for vasculitis.

LVV is reported to have been induced by anti-TNF treatment.

Whilst tocilizumab effectively controlled vasculitis but the young man continued to have bowel symptoms a second biologic, Vedolizumab was maintained. Further research into LVV and IBD is required.
Paediatric Inflammatory Bowel Disease in South Asian children in New Zealand: Increasing in incidence with a More Severe Phenotype

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Objectives and Study: Second-generation immigrant South Asian (SA) children have been hypothesised to have a higher incidence of paediatric-onset inflammatory bowel disease (pIBD) than non-South Asian children (NSA). Descriptive phenotypic data on pIBD in SA children in New Zealand are scarce.

Methods: In this retrospective cohort study, data on all children presenting with pIBD to a tertiary paediatric centre in New Zealand between January 2010 to June 2021 were collected. Disease phenotype, biochemical markers, clinical characteristics, clinic remission following exclusive enteral nutrition (EEN), clinical remission rates at 3 and 12 months, biologic use, and disease complications (rates of surgery and hospital admission) were compared. The incidence, clinical characteristics and outcomes were compared between SA and NSA children.

Results: 100 (20 SA; 80 NSA), 36 (9 SA; 27 NSA) and 10 (3 SA; 10 NSA) children had Crohn’s disease (CD), ulcerative colitis (UC) and inflammatory bowel disease unclassified (IBD-U) respectively. SA children were over-represented in this cohort compared to their demographic representation in the overall population (22.7% versus 8.7%, p=0.04). pIBD incidence was greater in SA children compared to NSA children (15.55 SA vs 4.63 NSA per 100,000; p=0.03). pIBD incidence increased by 6.1%/year (p=0.007) during this period, accounted for primarily by the rising incidence in SA children compared to NSA children (15.55 SA vs 4.63 NSA per 100,000; p=0.03). pIBD incidence increased by 6.1%/year (p=0.007) during this period, accounted for primarily by the rising incidence in SA (SA 16.8% p=0.01; European 2.7% p=0.317; Other Ethnicities 4.5%, p=0.309).

SA children with CD had higher rates of complex perianal disease (35% vs 16%, p=0.06) and well-formed granulomata on histology (75% vs 49%, p=0.03). SA children with UC were more likely to present with Paris S1 classification severe disease (78% vs 40%, p=0.05). SA children were found to have worse biochemical markers at presentation and lower rates of clinical remission as summarised in the table below.

<table>
<thead>
<tr>
<th>Biochemical Markers At Presentation (Mean)</th>
<th>South Asian n=32</th>
<th>Non-South Asian n=114</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferritin (mcg/L)</td>
<td>10</td>
<td>39</td>
<td>0.028</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>102</td>
<td>112</td>
<td>0.016</td>
</tr>
<tr>
<td>Vitamin D Deficiency (25OH Vit D &lt;50)</td>
<td>82%</td>
<td>31%</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Response to Induction and Maintenance Treatment

- Clinical remission following EEN (CD): 37.5% vs 61.5%, p=0.08
- Clinical remission following standard dose biologic induction: 42% vs 72%, p=0.042
- Clinical remission following biologic dose escalation: 43% vs 29%, p=0.22
- Clinical remission 3 months post-diagnosis: 40% vs 66%, p=0.015
- Sustained clinical remission 12 months post-diagnosis: 22% vs 54%, p=0.003

Conclusions: Increasing incidence of pIBD was disproportionately represented by SA children who had a more severe phenotype at presentation and followed a more severe disease course with lower remission rates following EEN and biologic therapy. Further evaluation of longer-term outcomes in these patients is required.
Dermatological manifestations in paediatric inflammatory bowel disease: a single centre experience in Northern Italy

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Objectives and Study: Skin manifestations are present in 10-15% of paediatric patients with inflammatory bowel disease (IBD). The frequency is higher in Crohn's Disease (CD) compared to ulcerative colitis (UC). Cutaneous lesions generally mirror underlying intestinal activity. The aim is to describe the cutaneous manifestations in our cohort of paediatric IBD patients in "V. Buzzi" Children's Hospital in Milan, Italy.

Methods: A retrospective analysis of clinical records (n=210) from January 2016 to May 2022 was performed to collect data on cutaneous manifestations in our cohort of patients with IBD, aged 6-18 years.

Results: A total of 28/210 (13.3%) patients presented with cutaneous manifestations; 23/28 (82.1%) had CD, 5/28 (17.8%) had UC. A total of 26/210 (12.4%) had oral or perianal lesions; 23/26 (88.4%) had CD; the most frequent localizations were retroauricular but also scalp, elbows, knees and umbilicus. No case was induced by anti-TNFα.

Four patients (4/28, 14.3%) had erythema nodosum (EN, 3/4 CD, 1/4 UC), all were female with colonic involvement. In all cases remission was obtained with oral prednisolone.

Two patients (2/28, 7.1%) had hidradenitis suppurativa (HS). One case (17-year-old girl, UC) was with inguinal HS which responded to oral doxycycline. The other case (16-year-old boy, CD) was axillary HS treated with IFX 5mg/kg every 4 weeks and topical clindamycin.

One case of pyoderma gangrenosum (1/28, 3.6%) of the leg in a 7-year-old boy with acute severe UC refractory to steroids and IFX, who underwent colectomy. One case of vitiligo (17-year-old girl, CD) at hands and knees treated with topical tacrolimus. One case of alopecia areata in a 14-year-old ileo-cecal CD. One case of recurrent vesicular-pustular rash in a 7-year-old girl with ileo-colonic CD (negative VZV-CRP and serological tests). Four cases of non-specific rash: a cutaneous small-vessel vasculitis (CD), recurrent urticaria in a non-atopic subject (CD), eczematous dermatitis at trunk, elbows and knees (CD), a non-specific macular rash at trunk accompanied by fever, aphthous stomatitis and penile vesicles in a 10-year-old patient with ileo-colonic CD. One case of genital abscess in a 14-year-old girl with active UC. Corticosteroid induced manifestations included 3 cases (2 CD, 1 UC) of severe acne, 1 case of face and scalp folliculitis and 3 cases of striae rubrae (2 CD, 1 UC).

Oral manifestations included: 1 case of gingivitis, 1 case of painful oral ulcers and 3 cases of aphthous stomatitis; all had CD. Perianal manifestations included: perianal fistulas in 11 cases (all CD), perianal fissures in 3 cases (2 CD, 1 UC) and skin tags in 7 cases (5 CD, 2 UC).

Conclusions: In our cohort of paediatric IBD patients the prevalence of skin manifestations is similar to data in literature (13.3%) and more frequent in CD compared to UC. The most common manifestations are psoriasis and reactivation lesions following intestinal activity (EN). In our cohort, skin manifestations were not accompanied by rheumatological symptoms except for one case of CD with arthritis of the ankle and EN at disease onset. No cutaneous manifestation was related to malnutrition, anti-TNFα treatment, malignancies or opportunistic infections.
Vaccination in pediatric inflammatory bowel disease – experience of a portuguese tertiary center


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Objectives and Study: Pediatric Inflammatory Bowel Disease (IBD) management involves a growing use of immunomodulators and immunosuppressor drugs. Immunosuppression has a major beneficial therapeutic effect in IBD. However, an increased risk of infection is one of the main complications associated to these drugs. Nonetheless, given the fact that part of this risk can be attenuated by vaccination, it is essential to promote and routinely assess the vaccination status of these patients.

We aimed to characterize vaccination status of a cohort of pediatric patients under current treatment for IBD.

Methods: Retrospective analysis of a cohort of pediatric patients with IBD diagnosis between april/2010 and april/2022 and currently in treatment in a Pediatric Gastroenterology Unit. Review of clinical records was performed. Demographic and clinical data were retrieved, with a particular focus on the vaccination records.

Results: 99 patients were included, 62.6% were male. Median age at diagnosis was 13 years old (IQR 11-15) and the mean follow up time 31 months. 100% of the patients had the primary national immunization program up-to-date at the time of diagnosis. Regarding additional vaccination, 68.7% had at least 1 seasonal flu vaccine during the follow-up period. 73.7% had the conjugated anti-pneumococcal vaccine (Prevenar 13®) and 63.6% the polysaccharide antipneumococcic vaccine. (Pneumovax 23®). 63.6% had Hepatitis A vaccine (individually or in conjunction with hepatitis B vaccine) and 60.6% had a Hepatitis B vaccine booster individually or in conjunction with hepatitis A vaccine). 54.2% of the patients without history of varicella (chickenpox) or positive serologies had the vaccination against varicella. Only 6% of the male patients (but 100% of the female due to inclusion in the national immunization plan) had human papilloma virus vaccine. 62.6% of the patients were vaccinated against SARS-CoV2 infection.

Conclusions: Vaccination and infection prevention are important issues in the follow-up of IBD patients. This study shows that, despite a good vaccination coverage comparing to previous international studies, there is still room for a significant improvement in this area. This reflects the need for and importance of immunization status review in all the follow-up visits and promoting vaccination of these patients. Diminishing barriers and facilitating access to vaccination are essential to achieve higher rates.
Diagnostic delays in paediatric inflammatory bowel disease and the impact of Covid-19 pandemic on the incidence of the disease in North-eastern Slovenia

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Objectives and Study: There is not much data about the diagnostic delays in paediatric inflammatory bowel disease (IBD), but it is known that in paediatric Crohn’s disease unrecognized disease might cause serious growth impairment. The Covid-19 pandemic posed many challenges in the management of patients with IBD since medical care was focused on patients with Covid-19 and was therefore restricted for other patients in many areas around the world.

The aim of our study was to calculate diagnostic delays and assess weight and height of children with IBD at the confirmation of diagnosis. We also studied changes in the incidence of paediatric IBD in North-eastern (NE) Slovenia during the ten-year period, with a special focus on the Covid-19 period.

Methods: A retrospective, single centre observational study was conducted in a cohort of children and adolescents (<19y) diagnosed with IBD between 2012 and 2021 in NE Slovenia. The observed time interval was divided into a pre-Covid-19 period (period one: 2012-2015 and period two: 2016-2019) and Covid-19 period (2020-2021). Annual incidence rates of Crohn’s disease (CD) and ulcerative colitis (UC) were calculated and disease activity index, diagnostic delays (duration from first symptoms to confirmation of diagnosis) and z-scores for weight and height of children with IBD (based on the WHO reference) at the time of diagnosis were determined. The results were compared between disease groups and according to the chosen time periods.

Results: During the study period, 73 IBD patients (52.1% female, mean age 15 years, 52% UC, 4% intermediate colitis) were diagnosed in NE Slovenia.

Median diagnostic delay from first symptoms to confirmation of diagnosis was 2 months (range 0m-3y; CD 3m (range 0m-3y); UC 1.5m (range 0m-22m); NS). There were no differences in diagnostic delays according to the time periods (period one and two 2m, Covid-19 period 2.8m, NS).

At the time of diagnosis, median z-score for weight of children with IBD was -0.15 (min -3.05; max 2.55) and for height 0.4 (min -1.72; max 2.53). CD patients were found to have slightly lower weight compared to UC patients (median z-score for weight: -0.4 vs 0.1, p<0.05). However, disease activity was higher in UC patients compared to CD patients (mean PUCAI 38 (min 15, max 65); mean PCDAI 28 (min 5, max 60); p<0.05). There were no differences in z-scores for weight and height and disease activity between chosen time periods.

Mean annual incidence of IBD (per 100.000) was 5.2 (95 % CI 3.4-7.1; CD 2.2 (95 % CI 1.0-3.6), UC 3.0 (95 % CI 2.1-3.9); NS). During the Covid-19 period the incidence of IBD has risen significantly (p<0.05) compared to the previous two periods (9.1 vs 4.2 respectively).

Conclusions: Diagnostic delays in paediatric IBD are relatively short in NE Slovenia and remained short throughout the observed period, also during the Covid-19 pandemic. The disease had no major impact on the growth of most patients at the time of diagnosis. The incidence of IBD in NE Slovenia has increased significantly in the last ten years, especially during the Covid-19 pandemic.
A review of the factors affecting remission rates in a tertiary paediatric IBD cohort

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Objectives and Study: Inflammatory bowel disease (IBD) is a chronic condition that is commonly diagnosed in the paediatric patient cohort. Due to its relapsing-remitting nature, it is important to tailor the treatment to each patient and achieving good control as defined by treating to target which is a combination of symptom scores and objective markers including; faecal calprotectin, blood tests, drug and metabolite levels, radiological and endoscopy assessment.

The aims of this project are to identify the population of patients in remission in the IBD cohort and, to identify the factors which affect this, particularly frequency of contact with IBD services.

Methods: A retrospective review was carried out using the data available on electronic hospital records. The data included: patient demographics, type of treatment, most recent biochemical and radiological assessment results and hospital visits from paediatric IBD patients at a National Health Service (NHS) hospital. All IBD subtypes were included. A Microsoft Excel spreadsheet was used to collect the data which was then reviewed by a senior consultant and subsequently analysed.

Results: In total, 150 patients were included. 72.67% of these patients were either found to be in remission or had mild disease activity. Higher remission rates/mild disease activity was observed in patients who had seen a consultant and had biological tests done within 6 months (90.63%) as opposed to patients who had not (38.46%). More patients receiving combination treatment of either aminosalicylates/a biologic and an immunosuppressant were found to be in remission than patients receiving just one or none of these treatments.

Conclusions: There appears to be a link between remission rates and local factors including: frequent monitoring through biological and radiological assessments, consultation visits and the type of treatment. Frequent monitoring of IBD patients may lead to higher remission rates. This can be achieved via frequent consultation reviews to include up to date scoring indices, biochemical and radiological assessment.
Faecal calprotectin remission within the first year of diagnosis is associated with a reduction in hospitalisation and surgery in children with Inflammatory Bowel Disease

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Objectives and Study: Faecal Calprotectin (FCP) remission is considered an adjunctive goal in treatment to target algorithm in patients with Inflammatory bowel disease (IBD). A recent study reported improved longitudinal outcomes in adults with Crohn's disease (CD) achieving FCP remission within the first year of diagnosis. Our objectives were to compare longitudinal outcomes in children with IBD who reached or failed to achieve FCP remission within the first year of diagnosis.

Methods: We performed a retrospective analysis of children diagnosed with IBD between February 2011 and February 2020 at Perth Children’s Hospital, including those with a minimum follow-up of 24 months. Children with confirmed IBD and the first measured FCP >250 µg/gm within 3 months of diagnosis (FCPbaseline) and at least one follow-up FCP done between 3 - 12 months (FCPfollow up) while on treatment were included for analysis. In children with multiple follow-up FCP, the value closer to 12 months was utilised for defining response. FCP response was classified as; FCP-normalisation (FCP-N, FCP< 100 µg/gm), FCP remission (FCP-R<250 µg/gm) and FCP non-remission (FCP-NR>250 µg/gm). The main outcomes of interest were cumulative rates of IBD-related hospitalisation and surgery (resection or seton/abscess drainage) at or after 12 months from diagnosis to the last follow-up. Outcomes were compared between groups with FCP-R(<250 µg/gm) and FCP NR(>250µg/gm) using the Fisher exact test and Kaplan Meier survival analysis.

Results: A total of 152 children (83 CD/65 UC/4 IBDU) with a median follow-up of 48 months (95% CI, 49.7 -58.7) were included for final analysis. An overall FCP response rate in our cohort was (52/152 (34%) normalisation, (79/152(52%) remission and (73/152(48%) non-remission. Baseline characteristics at diagnosis including disease phenotype, complicating behaviour, biomarkers value (CRP, ESR, FCP), severe endoscopic disease activity defined by large or deep ulcers or severe colitis and cumulative exposures to biologics were similar between the group with FCP-R vs. FCP-NR. Cumulative rates of hospitalisation and surgery beyond the first year of diagnosis were significantly lower in those with FCP-R (7/79(8.8%) vs. FCP-NR (31/73(43%), p=0.0001. Individual outcomes of hospitalisation (5/79 vs 20/73, p=0.0008) and IBD-related surgical intervention (2/79 vs.11/73, p=0.007) were also significantly lower in those with FCP-R vs. FCP-NR. (Figure1-Risk of surgery/hospitalisation in those with FCP remission vs. FCP non-remission). No significant difference was noted in the composite outcome of hospitalisation and surgery rates in those with FCP-Normalisation (3/52,5.7%) vs. FCP-Remission (7/79, 8.8%). A sub-group analysis of the cohort including only those commencing biologics within the 12 months of diagnosis as a proxy of more severe disease (64/152,42%) revealed similar longitudinal benefits on disease trajectory, with a reduction in combined hospitalisation and surgery (4/33 vs.19/31, p=0.0001) in those with FCP-R vs. FCP-NR.
Conclusions: Faecal calprotectin remission within the first 12 months of diagnosis may influence longitudinal disease trajectory with a sustained reduction in both hospitalisation and IBD surgery in children with IBD over a median follow-up of 4 years. Prospective paediatric studies examining longitudinal disease trajectories in those attaining early FCP remission will offer definitive evidence of this biomarker's prognostic utility.
Improvement of transmural inflammation with adalimumab versus immunomodulator maintenance therapy in pediatric Crohn’s disease: single-center prospective evaluation using PICMI

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Objectives and Study: Magnetic resonance enterography (MRE) is increasingly used to assess transmural inflammation and damage in children with Crohn’s disease (CD) involving the small intestine, but data are limited concerning efficacy of existing therapies in achieving transmural healing. The recently developed pediatric MRE-based multi-item measure of inflammation (PICMI) was utilized in a prospective study examining the efficacy of adalimumab (ADA) and immunomodulator (IM) maintenance therapy in ameliorating transmural inflammation.

Methods: In this single-centre longitudinal cohort study, eligible patients were children aged <17 years with CD involving small bowel on MRE and planned initiation of ADA or IM as maintenance therapy. Clinical, anthropometric and laboratory data were prospectively collected at baseline, at end of the induction (with prednisone/exclusive enteral nutrition/ADA), and at 6 and 12 months. A single radiologist scored both MREs in random order, blinded to any clinical information. MRE items scored included segment length, wall thickness, wall T2 hyperintensity, wall diffusion restriction, mural ulcers, comb sign, fat stranding/mesenteric edema, penetrating disease, stricture, and global assessment. Primary outcome planned at study inception was improvement in inflammation on MRE as judged by radiologist global assessment. The simplified MRE index of activity (MARIAs) (Ordas, Gastroenterology 2017) and the PICMI were calculated for the small bowel as secondary outcomes by summing the segmental scores for the terminal, distal, and proximal ileum, and jejunum. Patients who escalated maintenance therapy during follow-up were considered as treatment failures on an intent to treat basis. We compared groups using chi-square, Fisher’s exact test, Mann-Whitney U or related-samples Wilcoxon signed rank tests as appropriate.

Results: Between 10/2015 and 10/2019, 62 eligible patients were enrolled, 26 receiving ADA and 36 IM. Patients treated with ADA had more extensive CD (more often L3 and L4b), and more severe baseline disease activity based on physician global assessment (PGA) and Paediatric CD Activity Index (PCDAI) (Table 1). Of the 62 patients enrolled, 46 continued their initial maintenance therapy for 1 year. 14 (39%) patients started on IM required early therapy escalation due to unsatisfactory symptom control, while only 2/26 (8%) receiving ADA required treatment change (p=0.006). Median ADA trough levels during maintenance 12 ug/ml (IQR 10.6-13.5). Of the 46 patients continuing initial maintenance therapy, 41 had a follow-up MRE at 12 months. By radiologist global assessment, on an intent to treat basis, 71% of the ADA vs. 42% of the IM group improved (p=0.03). A decline in PICMI score of >20 points was observed more frequently in ADA-treated patients compared to those receiving IM (54% vs 31%, p=0.01). Conversely, MRE normalization was rare and rates were similar between groups (9% vs 6%, p=0.62).
<table>
<thead>
<tr>
<th></th>
<th>Overall (n=62)</th>
<th>ADA (n=26)</th>
<th>IM (n=36)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>45 (73%)</td>
<td>19 (73%)</td>
<td>26 (73%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>13.5 (11.9, 15.3)</td>
<td>14.2 (13.3, 15.8)</td>
<td>12.9 (10.5, 15.0)</td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>Newly diagnosed (&lt;3 months)</td>
<td>55 (89%)</td>
<td>23 (89%)</td>
<td>32 (89%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Location: L1; L3</td>
<td>26 (42%); 34 (55%)</td>
<td>7 (27%); 17 (65%)</td>
<td>19 (53%); 17(47%)</td>
<td><strong>0.04</strong></td>
</tr>
<tr>
<td>additional L4b ± L4a</td>
<td>10 (16%)</td>
<td>7 (27%)</td>
<td>3 (8%)</td>
<td><strong>0.05</strong></td>
</tr>
<tr>
<td>Pre-induction wPCDAI</td>
<td>47.5 (27.5, 65)</td>
<td>53.75 (40, 65)</td>
<td>47.5 (27.5, 62.5)</td>
<td>0.56</td>
</tr>
<tr>
<td>Pre-induction hs CRP (g/L)</td>
<td>23.9 (11.8, 43.7)</td>
<td>33.1 (13.2, 65.5)</td>
<td>23.0 (11.5, 37.3)</td>
<td>0.34</td>
</tr>
<tr>
<td>Pre-induction Hb (g/L)</td>
<td>114 (101, 126)</td>
<td>104 (98, 115)</td>
<td>139 (131, 144)</td>
<td>0.81</td>
</tr>
<tr>
<td>Pre-induction FC (microg/g)</td>
<td>1444 (906, 1800)</td>
<td>1444 (602, 1800)</td>
<td>1053 (1025, 1427)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

**Conclusions:** ADA therapy was associated with objective improvement in MRE findings of inflammation more frequently than IM. The low rate of MRE normalization suggests, in accordance with STRIDE-2 guidelines (Turner, Gastroenterology 2022), that this is not yet a realistic target with existing therapies.

**Conflict of Interest:** **AMG:** consultant Abbvie, Amgen, BristolMyersSquibb, Janssen, Lilly, Merck, Pfizer, Takeda; speaker fees Abbvie, Janssen, Nestle.

**MLG:** AbbVie grant, AbbVie and Samsung speaker honoraria

**PC:** Educational grants from Abbvie, Amgen, Janssen, Takeda, Viatris; Speaker fees from Abbvie, Amgen; Consultant fees from Abbvie, Amgen, Ferring, Merck
Early pro-active therapeutic drug monitoring is associated with greater durability of infliximab response: a single center comparative analysis

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Objectives and Study: The value of proactive infliximab (IFX) therapeutic drug monitoring (pro-TDM) during maintenance has been controversial (Ricciuto, JCC 2018), but implementation during or immediately following induction is increasingly utilized to allow early personalization of dose. We evaluated the impact of pro-TDM prior to first maintenance dose on durability of IFX response in children with IBD.

Methods: This was a single-center retrospective study including all children and adolescents receiving IFX via 3-dose induction as first biologic to treat luminal IBD between 2001 and 2018 at SickKids Hospital, Toronto. Beginning 09/2013, based on experience with early loss of responsiveness (LOR), we planned early administration of first IFX maintenance dose (week 12 rather than customary week 14 for ambulatory patients; week 8 following intensified induction for hospitalized patients with acute severe ulcerative colitis). Pro-TDM prior to first maintenance dose guided personalization of dose and dosing interval aiming for target trough levels of >/=10 mcg/mL. Patients initiating IFX with early pro-TDM were matched for baseline characteristics with controls managed without early pro-TDM using propensity score (PS) matching method. One-to-one matching was done using the nearest neighbor method without replacement. Secondary LOR was defined as loss of benefit necessitating IFX discontinuation after initial response. Rates of IFX secondary LOR were compared between the groups using Kaplan-Meier (KM) survival analysis and differences appraised with the log-rank test. Predictors of secondary LOR were evaluated by univariate Cox-regression in the matched cohort, and by multivariate regression in all IFX-treated patients.

Results: From the 520 IFX-treated patients identified, of which 180 (34.6%) received IFX with early pro-TDM, 156 PS matched pairs were created. Potential confounding variables for PS calculation were sex, ethnicity, type of IBD, disease location according to Paris classification, disease duration, use of concomitant immunosuppressants and the use of an intensified induction regimen. Of the 312 matched patients (median age 12 years; IQR: 2 years), 173 (55.4%) were male, 159 (51%) had Crohn’s disease (CD). Median disease duration was 10 months (IQR: 16 months). 282/312 matched patients responded to the induction therapy. After PS matching, no difference in baseline characteristics was observed between patients who received IFX with or without pro-TDM. 26/282 (9.2%) of the primary responders experienced subsequent secondary LOR, but PS matched patients who received IFX with pro-TDM had lower rates of secondary LOR compared to those who received IFX without pro-TDM (Figure 1, Log-rank test p=0.009). In univariate Cox-regression analysis, pro-TDM (HR: 0.37, 95% CI: 0.16-0.86, p=0.021) and the achievement of complete clinical remission at the end of induction (HR: 0.31, 95% CI: 0.14-0.69, p=0.004) were associated with reduced risk of secondary LOR. Further, these factors alone were similarly influential among the entire cohort of 520 IFX-treated patients (HR: 0.33, 95% CI: 0.17-0.66, p=0.002 and HR: 0.38, 95% CI: 0.21-0.67, p<0.001).
Conclusions: Our results support regimen adjustment based on early proTDM as a strategy to improve durability of IFX responsiveness in pediatric IBD

Conflict of Interest: TW: consultant for Abbvie and Janssen; speaker fees from Abbvie, Janssen, Nestle.
AMG: consultant Abbvie, Amgen, BristolMyersSquibb, Janssen, Lilly, Merck, Pfizer, Takeda; speaker fees Abbvie, Janssen, Nestle.
PC: Educational grants from Abbvie, Amgen, Janssen, Takeda, Viatris; Speaker fees from Abbvie, Amgen; Consultant fees from Abbvie, Amgen, Ferring, Merck.
All the other authors have no COI to disclose.
P-111

Non-invasive assessment of efficacy of exclusive enteral nutrition using composite score of faecal calprotectin, CRP, weighted PCDAI and Mucosal Inflammation Non-invasive Index (MINI) in Paediatric Crohn’s disease – the Indian experience

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Objectives and Study: Exclusive enteral nutrition (EEN) is recommended as first line therapy for induction of remission in active luminal paediatric Crohn’s disease (CD). There is paucity of data regarding use and efficacy of EEN from India. We aimed to assess efficacy of EEN in paediatric CD non-invasively using a composite score of faecal calprotectin, CRP, clinical scores such as Pediatric Crohn’s disease activity index (PCDAI) and weighted PCDAI (wPCDAI) and Mucosal Inflammation Non-invasive index (MINI).

Methods: Between 2020-2022, consecutive patients <18 years of age, diagnosed with CD based on Porto criteria, who received EEN for at least 2 weeks were included. Patients who received steroids or biologics were excluded. Demographics, distribution and severity of disease at diagnosis were recorded. Growth parameters, haematocrit, CRP, ESR, platelet count, albumin and faecal calprotectin were recorded, and PCDAI, wPCDAI and MINI scores were calculated at baseline and at completion of EEN (6 or 8 weeks). Clinical remission (CR) was defined as PCDAI <10 or wPCDAI <12.5. Clinical response was defined as a decrease in PCDAI of > 12.5 and wPCDAI > 17.5 points. Tolerance and compliance to EEN was recorded at every visit until completion of EEN.

Results: 26 patients (11,42% male) were included. Majority of patients had ileocolonic disease (L3,54%) and moderate-to-severe CD based on PCDAI >30 (69.2%), wPCDAI >57.5 (65.3%) and MINI >11 (89.5%). 38.4% (10/26) were moderate to severely malnourished based on weight for age Z score and BMIZ score at diagnosis. 53.8% (14/26), 42.3% (11/26) and 3.8%(1/26) of patients received polymeric, semi-elemental and elemental formula respectively. Mean duration of EEN therapy was 7.9 weeks (IQR 6.1-8.9). At completion of EEN, a comparison between baseline and post EEN variables showed that 80.8% (21/26) patients had significant improvement (figure 1) in height for age Z score (-0.7 ± 1.2 to -0.5 ± 0.9, p=0.03), BMI Z score (16 ± 3.7 to 17.5 ± 2.8, p<0.005), haematocrit (33% ± 5.3 to 38.8 % ± 2.2, p<0.005), platelet count (565 x10^3/µL ± 221.9 to 365 ± 79.3 x10^3/µL, p<0.005) and serum albumin levels(3.4 ± 0.6 to 4.2 ± 0.4 g/dL, p<0.005). 80.8% (21/26) patients achieved clinical remission. Tolerance and compliance to EEN was good. Five (19.2%) patients failed EEN with no clinical response despite 2 weeks of EEN. Median duration of follow-up was 9 months (IQR 5-12.2). 90.4% (19/21) of patients who achieved remission with EEN remained in steroid free clinical remission on azathioprine maintenance therapy for the duration of follow-up. 2 patients required escalation to biologics at 16 months and 12 months for thiopurine failure and fistulising disease respectively.
Figure 1. Box plots showing differences in WAZ score, CRP, wPCDAI, calprotectin and MINI index pre and post EEN.

Conclusions: Exclusive enteral nutrition induced clinical remission in 80.8% of Indian children with CD. 90.4% of patients who achieved remission with EEN remained in steroid free clinical remission for the duration of follow-up. In TB-endemic countries such as India, we suggest use of EEN as first line induction agent given its nutritional benefits and lack of adverse effects such as those seen in anti-tubercular therapy. These results need to be confirmed in large cohorts in a prospective manner.
10 Years of Biological Therapy in Paediatric Inflammatory Bowel Disease: experience from a tertiary centre

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Objectives and Study: The advent of biological therapy has greatly improved the treatment of inflammatory bowel disease (IBD) in both paediatric and adult populations. The aim of this study was to describe the cumulative experience of biological treatment practice in paediatric IBD, within the last ten years (2011-2022) in a single tertiary centre.

Methods: A retrospective chart review of paediatric IBD patients (≤ 18 years) in whom biological therapy was initiated. Demographics, biological therapy indication, drug monitoring data, side effects and clinical efficacy data, were analysed.

Results: From a total of 132 patients, 32 required biological therapy (24%) (23 with Crohn’s disease (CD), 8 with ulcerative colitis (UC) and 1 with IBD unclassified). The most frequent indications for biological initiation in CD, were stricturing disease 9 (39,1%), perianal disease 6 (26,1%), first-line therapy failure/intolerance 6 (26,1%), penetrating disease 1 (4,3%); in UC it was severe steroid-refractory disease 8 (100%).

The initial agent was infliximab (IFX) in 56,3% (CD 10, UC 8) and adalimumab (ADA) in 43,8% (CD 13, IBD unclassified 1). The mean time from diagnosis to biological agent initiation was 2,6 years (min 0,1; max 12,92). Initial clinical remission at 16 weeks was achieved in 23 patients (71,9%): 9 ADA-treated patients (69,2%, all with CD) and 14 IFX-treated patients (77,8%, 5 UC, 9 CD). Nine of the patients (4 ADA-treated (3 CD, 1 IBD unclassified) and 5 IFX-treated (4 UC, 1 CD)) were primary non-responders. Another 5 (3 ADA-treated (2 CD, 1 IBD unclassified) and 2 IFX-treated (1 CD, 1 UC)) were secondary non-responders and the last 3 had switched, due to cutaneous side- effects (3 ADA-treated, all CD). A second biological agent was initiated in 16 patients (50%). The mean time to second agent initiation was 2,8 years (min 0,3;max 6,32), 3,6 years in ADA-treated patients and 1,8 years in IFX-treated patients. In patients who maintained first-line therapy (50%), the mean duration of treatment was 6,51 years (min 3,72;max 9,53), 5,63 years in ADA-treated and 6,91 years in IFX-treated patients.

Vedolizumab was introduced as the second-line agent in 5 patients (3 UC, 2 CD), ADA in 4 (2 UC, 2 CD), IFX in 4 (3 CD, 1 IBD unclassified) and ustekinumab in 3 (3 CD). Clinical remission occurred in 2/3 of vedolizumab-treated patients, 0/4 ADA-treated, 3/4 IFX-treated patients and 1/3 ustekinumab-treated patients. Six patients switched to a 3rd biological agent (in all cases to vedolizumab); of these, 2 entered into clinical remission and 4 switched to a 4th agent (3 to ustekinumab and 1 to tocilizib). Drug monitoring was performed in 96,9% of patients, the levels were low in 34,4% of patients (ADA 15,4%, IFX 50%) at some point during the treatment and 4 patients (12,5%)developed antibodies (3 patients with IFX and 1 with ADA). During the study period, a total of 12 patients (37,5%) have undergone surgery: 2 with UC due to medical therapy failure and the remaining 10 with CD, (6 with a persistent stricture and intestinal obstruction, 2 with penetrating disease and perianal fistulae and another 2 with colic abscesses).

Conclusions: In our experience, biological therapy was safe and allowed a successful long term disease control in a great proportion of patients; however, multiple agents and/or surgery was required in a few patients with severe disease.
Moderate Correlation between Nancy Histopathology Index and Clinical, Laboratory and Endoscopic Indices of Disease Activity in Pediatric Patients with Ulcerative Colitis

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Objectives and Study: Different histologic scores are used to assess disease activity among adult patients with ulcerative colitis (UC), including the Geboes Score, the Robarts Histopathology Index, and the Nancy Histopathology Index (NHI). However, these indices are not validated in pediatric patients and typically not used in clinical practice in children with UC. Our goal was to determine whether the NHI correlates with different clinical, laboratory and endoscopic indices of disease activity in pediatric UC.

Methods: Clinical, laboratory and endoscopic data was collected from all patients with UC aged <18 years that underwent a colonoscopy or a sigmoidoscopy at Schneider Children's Medical Center between 2019-2020. When the patient had multiple endoscopies, only the first one was included. The NHI from the recto-sigmoid region was scored by a single senior GI pathologist, and ranged between 0 (no histologic activity) and 4 (severe inflammation). The Kendall's tau-b test was used to determine correlation between NHI and the Mayo Endoscopic Score (MES), while Spearman's rank correlation coefficient test was used to determine correlation with the Pediatric Ulcerative Colitis Activity Index (PUCAI), albumin, CRP and calprotectin values.

Results: Data was collected from 61 UC patients (34 [55.7%] with a new diagnosis), 34 females (55.7%), with a median age of 14 years (IQR 11-15 years). Among patients with prior diagnosis of UC, the median time from diagnosis to endoscopic procedure was 49.5 months (IQR 20-60.6). Thirteen percent presented with acute severe colitis and 26.1% were in clinical remission. The median PUCAI score was 30 (5-55), while the median albumin, CRP and calprotectin values were 4.3 g/dL (IQR 4.0-4.5), 0.2 mg/dL (IQR 0-0.9) and 778 mg/g stool (IQR 274-2,012), respectively. Ten patients (16.4%) had a MES of 0 (endoscopic remission), while 17 patients (27.9%) exhibited a MES of either 1, 2 or 3. The NHI was 0, 1, 2, 3 and 4 in 7 (11.5%), 3 (4.9%), 2 (3.3%), 41 (67.2%) and 8 (13.1%), respectively. No significant correlation was found between albumin or CRP values and NHI. However, a positive moderate correlation was identified between NHI and PUCAI score (r=0.6, P<0.001), and between NHI and calprotectin levels (r=0.54, P=0.001) values. Moreover, there was also a significant positive correlation between the NHI and MES (r=0.54, P<0.001).

Conclusions: We demonstrate a significant moderate positive correlation between NHI and different markers of disease activity, including PUCAI, calprotectin and MES. Given the increasing interest in linking histologic activity with outcomes in patients with UC, additional studies are needed in pediatric patients to determine its utility and predictive value in clinical practice.
Symptom self-reporting in Paediatric IBD: the feasibility of use for disease activity monitoring and unique paediatric considerations

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Objectives and Study: The Pediatric Crohn’s Disease Activity Index (PCDAI) and Pediatric Ulcerative Colitis Activity Index (PUCAI) continue to be a key tool for disease monitoring in paediatric Inflammatory Bowel Disease (pIBD). These DAI’s are amenable to translation into patient reported outcome (PRO) questionnaires; here, we evaluate the utility of a PRO in our pIBD population and explore some of the unique aspects of using a PRO in paediatrics.

Methods: This is a study of prospectively collected data gathered as part of a quality improvement initiative through the IBD program at British Columbia Children’s Hospital in Vancouver, Canada. From May 2014 through June 2018, an iPad-based REDCap survey was filled out by patients (age 7.2 – 18.6, median 15.1 yrs) at routine clinic and infusion visits. The survey included a set of 9-19 questions, depending on the patient’s response to questions and whether they had CD or UC/IC; REDCap calculated PCDAI and PUCAI scores for each survey, with UC and IC both using the PUCAI. Disease characteristics and physician-calculated DAI scores were obtained for the corresponding visit from the medical chart. To look at Quality of Life (QoL), the PedsQL™ 4.0 generic scale was included and scored using a likert scale.

Results: 826 surveys were completed by 328 patients (605 CD, 221 UC/IC, median 2 survey’s/patient). 587 (71.1%) were completed by patients without parental input, with 237 (28.9%) completed with the help of, or entirely by, the parent on behalf of their child. Overall, there was excellent agreement between the patient/parent (PRO) and physician (PH) scores, with a Pearson correlation coefficient of 0.711 for PCDAI (p<0.001) and 0.861 for PUCAI (P<0.001). The level of agreement varied by disease activity, with those in clinical remission having an equivalent score 84.7% (CD) and 73.2% (UC) of the time, decreasing to 66.5% (CD) and 49.0% (UC) in patients with active disease. When discordant scores existed, 78.7% (CD) and 81.0% (UC) of the time the PRO score was higher than the PH score. Notably, PRO’s were more often equivalent to PH scores when completed by the patient (vs. by parents). With discordant scores (PUCAI and PCDAI), patients scored themselves higher than the physician 16.2% of the time while parents scored their children higher 27.1% of the time. Conversely, physicians scored patients higher than parents < 5% of the time. Most of this difference came from abdominal pain reporting: compared to PH scores, higher abdominal pain scores were reported in 27.8% of parent surveys, vs. 17% of patient surveys. Mean QoL scores for patients decreased from 86.7 for patients in remission, to 74.8 and 67.8 with mild and moderate-severely active disease respectively (ANOVA p<0.001). The survey asked about medication adherence and were flagged for responses of “sometimes” or “usually” forgetting to take a medication. For patients taking methotrexate (n=192), 33% were flagged; however, for parent-completed surveys, 13% were flagged vs. 41% when patients completed their own. For patients on azathioprine (350 surveys), adherence concerns were flagged in 45% (48% for patient and 40% for parent surveys).

Conclusions: This large cohort of paediatric patients demonstrates feasibility and reliability of PRO’s in pIBD, with unique considerations for use in this population.
Higher infliximab dosing is associated with superior drug durability and clinical outcomes in VEO-IBD - a retrospective cohort study

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Objectives and Study: Very early onset IBD (VEO-IBD) denotes the subpopulation of patients diagnosed before the age of 6 years, among whom colonic IBD predominates. Young children have distinct pharmacokinetics which may affect treatment efficacy. However, there are few reports on the use of biologic agents in this population. We aimed to describe our single center experience of biologic use in VEO-IBD, including treatment regimens used and clinical outcomes. Secondary objectives included exploring the relationship between anthropometrics and drug exposure in this population.

Methods: Retrospective cohort study of children diagnosed with IBD before age 6 yrs (excluding monogenic IBD), and treated with a biologic before 9 yrs, at a single center between 2010-2021. All patients had a minimum six month follow up. Infliximab dosing was examined in mg/kg and in mg/m². Primary non-response was defined as biologic cessation, surgery, or lack of clinical response by the start of maintenance. Secondary loss of response was defined as biologic cessation, surgery, or at least moderate clinical activity after achieving corticosteroid-free clinical remission.

Results: We identified forty-five children with VEO-IBD who were started on a biologic; 51.1% female, 87% colon-only IBD, with median age at diagnosis of 3.5 yrs (IQR 2.4-5.0). The majority of children received infliximab as first-line biologic (43/45), while vedolizumab was first-line in 2 children with coexisting primary sclerosing cholangitis. Median age at start of biologic was 5.58 yrs (IQR 3.8-7.2). There was concomitant immunomodulator use in 12 (26.7%). Infliximab dosing at the start of maintenance was median 8.68 mg/kg (IQR 5.8-11.0) or median 177.4 mg/m² (IQR 130.7-283.9). This did not change significantly over 1 and 2 yr follow up. All children received more than the standard 5 mg/kg dosing. Infliximab levels pre dose 4 were median 12.01 µg/ml (IQR 4.58-28.01). Ability to achieve drug level of greater than 10 µg/ml was significantly associated with induction dose of infliximab (median 10.1mg/kg (IQR 7.2-15.8) vs 5.8mg/kg (IQR 5.6-6.8), p=0.012; 256.2 mg/m² (IQR 178.2-366) vs 148.5 mg/m² (IQR 130.6-170.3), p=0.012). Infliximab cessation occurred in 44% and was due to primary non-response in 52.6% and secondary loss of response in 31.6%. Median time spent on first biologic was 217 days (IQR 149-471). Children who received infliximab dosing ≥10mg/kg (40%) were more likely to have remained on infliximab at 1 year (Fig). Corticosteroid free clinical remission on infliximab was achieved by 54% (20/37) at 6 months, 71.4% (20/28) at 1 year and 63.1% (12/19) at 2 years. Fourteen children progressed to a second line biologic: 42.8% ustekinumab, 28.6% adalimumab, 28.6% vedolizumab. Dual biologics were used in 3 children, after failing infliximab monotherapy. Colectomy was performed in 6 patients (13.3%) over a median follow up time of 765 (IQR 348-1955) days.
**Conclusions:** VEOIBD patients require higher infliximab dosing than standard 5mg/kg to maintain drug levels greater than 10µg/ml. Children receiving higher dosing are more likely to achieve target drug levels and to continue on infliximab treatment.

**Conflict of Interest: Peter Church:** Educational grants from Abbvie, Amgen, Janssen, Takeda, Viatris, Speaker fees from Abbvie, Amgen, Consultant fees from Abbvie, Amgen, Ferring, Merck
One-year outcomes with ustekinumab therapy in paediatric crohn’s disease: A multicenter cohort study

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Objectives and Study: Ustekinumab (UST) is an effective treatment for adults with moderate to severe Crohn’s disease (CD), however data are lacking in children. This study aimed to evaluate one-year outcomes of UST in children with CD.

Methods: Children 2-17 years-old with CD were prospectively followed from diagnosis or UST start or enrolled retrospectively if previously received UST into a multicenter cohort study at participating sites of the Canadian Children Inflammatory Bowel Disease Network (CIDsCaNN). Inclusion criteria were initiating UST for luminal CD between 21/04/2017 and 14/02/2017 and at least one year of follow-up on UST or stopping UST before one year. Children with missing wPCDAI and PGA at one-year were excluded. Primary outcome was one-year steroid-free clinical remission (SFCR) (defined by weighted Pediatric Crohn's Disease Activity Index [wPCDAI] score < 12.5, Physician Global Assessment (PGA) of no activity, no corticosteroid use in previous 28 days, no surgery, and continuing UST). Secondary outcomes were clinically inactive/mild disease activity at one year (defined by wPCDAI score <40, PGA of none or mild activity, no corticosteroid use in previous 28 days, no surgery and continuing UST) and association between response to UST and previous biologic exposure (measured by odds ratio [OR] and 95% confidence interval [CI]).

Results: Forty-seven children met inclusion criteria; two were excluded for missing disease scores. Our final cohort comprised 45 children with median age 15.2 (interquartile range [IQR] 12.7-16.3) years, 47% female, and median duration of CD 2.6 (1.4-4.0) years. Disease location was distal ileal cecal (25%), colonic (32%) and ileocolonic (39%) with predominantly non-stricturing, non-penetrating behaviour (91%); 38 (84%) children had previous anti-tumor necrosis factor therapy, including 2 (4%) with previous vedolizumab also.

All children received UST intravenous induction (median dose 6.3 [IQR 5.3-7.2] mg/kg) followed by initial maintenance dosing of 90 mg subcutaneous every 8 weeks. Median duration of follow-up on UST was 486 (IQR 350-796) days. At one year, 20 of 45 (44%) achieved SFCR, including 17 of 38 (45%) previously treated with biologics and 3 of 7 (43%) biologic naïve children (OR 1.08, 95% CI 0.16-8.40). Clinically inactive/mild disease activity was achieved by 33 (73%) children, including 28 (74%) previously treated with biologics and 5 (71%) biologic naïve (OR 1.12, 95% CI 0.09-8.30). Seven children stopped UST before one year at median 24.7 (IQR 11.0-43.4) weeks: 5 due to inadequate response (2 proceeded to surgery), 2 due to patient choice. Twenty-one children (47%) underwent escalation with interval shortening to 4 weeks; after escalation, 17 of 19 (89%) continuing UST achieved clinically inactive/mild activity at one year. Five children underwent re-induction at median time 48.9 (IQR 30.1-55.7) weeks. A small group of children underwent therapeutic drug monitoring; median UST level at week 8 was 6.5 ug/mL (IQR 4.5-10.2) [N=6], at week 16 was 3.0 ug/mL (0.7-6.3) [N=7] and at 12 (±3) months was 3.5 ug/mL (IQR 2.4-4.4) [N=7].

Conclusions: In a real-world Canadian multicenter cohort, UST demonstrates a clinical remission rate of 44% in children with CD and 73% had clinically inactive/mild disease activity at one year with no impact of previous biologic exposure on achievement of outcomes.
Early inflammatory bowel disease in a Portuguese Tertiary Center

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Objectives and Study: Early (EOIBD) and very-early onset (VEOIBD) paediatric Inflammatory Bowel Disease are challenging to gastroenterologist due to its broad clinical presentation and aggressive behaviour. Diagnosis is supported by clinic, endoscopic, histopathologic and molecular findings. Bowel imaging can add important information in characterization of disease phenotype. We aimed to characterize the clinical, therapeutic and radiological manifestations in EOIBD and VEOIBD patients.

Methods: Retrospective analysis of clinical files of patients diagnosed with EO/VEO-IBD on a Paediatric Gastroenterology Unit between April/2010 to April/2022 in current follow up. Demographic, clinical, molecular and radiological data were collected, valuing MRE findings.

Results: Over 12 years 27 cases of EO/VEOIBD were diagnosed (8 VEOIBD and one Infantile onset IBD) in a global sample of 99 patients (27%). The average age of symptom onset in EOIBD was 8.9 years (SD+0.94 years) and 4.2 years (SD+1.54) in VEOIBD. 30% had a family history of IBD. 70% of cases (n=19) had diagnosis of Crohn’s disease, 11.1% (n=3) of ulcerative colitis or indeterminate colitis (n=3) and two cases of monogenic disease (XIAP deficiency and IL-10 signaling defect). Small intestine study by MRE was performed in 15 patients (58%) and 7 patients had changes in small intestine. About 30.7% of patients had perianal disease and Crohn’s isolated colonic disease in only two cases.

The average follow-up time was 5 years (minimum 6 months, maximum 12 years). Comparatively, EO/VEOIBD had a rate of biologic therapy in 55.5% of cases and more than two biologics in 14.8% of cases (against 59% and 9% of the general sample). In one of the cases of monogenic disease, bone marrow transplant allowed complete remission of the disease.

Conclusions: EOIBD and VEOIBD are diagnostic and therapeutic challenges. The characteristics of our sample are similar with previously described, although with a lower incidence of indeterminate colitis and a slight higher rate of small bowel disease, with MRI playing a key role in the reclassification of indeterminate colitis.

The use of a high number of biologicals correlates with a more aggressive phenotype of the disease. The treatment of genetic defects can be successful by bone marrow transplantation.
Opportunistic infections in paediatric inflammatory bowel disease: the 12-year experience of a tertiary paediatric hospital


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Objectives and Study: The introduction of drugs with greater immunosuppressive potential in Inflammatory Bowel Disease (IBD) has significantly improved disease control. However, the risk of opportunistic infections is a major concern and there is an increasing focus on preventing, diagnosing and managing opportunistic infections in IBD.

There are no published studies on opportunistic infections in paediatric patients with IBD in Portugal. The objectives were to characterize opportunistic infections, their treatment and evolution in a sample of children and adolescents with IBD in a tertiary paediatric hospital.

Methods: Retrospective descriptive analysis of the clinical records of patients diagnosed between April 2010 and April 2022 in current follow-up at the Paediatric Gastroenterology Unit of a tertiary paediatric hospital.

Results: In the last 12 years, 99 patients with IBD were followed, most with Crohn’s Disease (CD) (69.7%), followed by Ulcerative Colitis (UC) (21.2%) and Unclassified Colitis (UnC) (9.1 %), with a predominance of males (62.6%). The median age at diagnosis was 13 years and the median duration of follow-up was 31 months.

We observed 16 opportunistic infections in 14 patients (corresponding to 12.1% of the total), 2 of them with 2 infections.

Opportunistic infections were, in order of frequency: Cytomegalovirus (CMV) infection (n=5), tuberculosis (n=2), chickenpox (n=2), Clostridium difficile infection (n=2), sepsis by Candida parapsilosis (n=1), CMV reactivation (n=1), Herpes zoster reactivation (n=1), local herpetic infection (n=1) and Epstein Barr virus infection (n=1).

Of the patients with opportunistic infections, 8 were diagnosed with CD (57.1%), 4 with UC (28.6%) and 2 with UnC (14.3%). All patients with opportunistic infection were treated with biological drug and/or immunomodulator.

In addition to symptomatic treatment, 15 received specific treatment. In 10 cases, hospitalization was required (62.5%), with a median duration of hospitalization of 17 days (minimum 4, maximum 80).

In 87.5%, there were no complications. We observed 1 case of hepatitis associated with CMV colitis and 1 case of catheter-based sepsis.

Conclusions: Opportunistic infections represent a challenge in the follow-up of IBD. In the studied sample, despite the negative impact due to the fact that the majority required hospitalization with intravenous treatment, the percentage of complications was low.

More studies in paediatric age are needed.
Treatment of inflammatory bowel disease in paediatric age: what about adverse reactions?


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Objectives and Study: The therapeutic approach to Inflammatory Bowel Disease (IBD) in paediatric age is complex, involving the use of different pharmacological classes. The main objective is to achieve remission with minimal adverse reactions (AR).

The objectives were to characterize the AR that occurred with drugs used in the treatment of IBD in paediatric age.

Methods: Retrospective analysis of patients records with IBD from April 2010 to April 2022 followed in a Paediatric Gastroenterology Unit.

Demographic and clinical data were collected, including drugs, occurrence and severity of AR, treatment and course.

Results: Ninety-nine patients were included, 62.6% male, with a median age at diagnosis of 13 (IQR: 11-15) years. Most (69.7%) had Crohn's Disease, followed by Ulcerative Colitis (21.2%) and Unclassified Colitis (9.1%). The most prescribed treatments were: immunomodulators (n=78; 78.8%), exclusive enteral nutrition (n=62; 62.6%), biological (n=58, 58.6%; infliximab in 46 (49.9%) and adalimumab in 14 (24.1%)), aminosalicylates (n=49; 49.9%), and corticosteroids (n=35; 35.4%).

During a follow-up of 31 (IQR: 11-51) months, 16 AR occurred in 15 (15.2%) patients, mostly at home (80%). The most implicated drug was azathioprine (n=11; 68.8%), and the AR included hepatitis (n=6; 37.5%), pancreatitis (n=3; 18.8%), myelosupression (n=2; 12.5%), gastrointestinal intolerance (n=1; 6.25%) and nephrotoxicity (n=1; 6.25%) in a patient with a history of chronic kidney disease.

One patient had hepatitis and another had severe neutrophilia and worsening colitis with mesalazine.
One patient experienced skin rash after administration of adalimumab and another psoriasis after infliximab.

Dose reduction was necessary in 6 (40%) and suspension in 13 (86.7%).

In most cases (87.5%) no specific treatment was needed; 1 patient was treated with ursodeoxycholic acid for cholestatic hepatitis and another on topical steroids for eyelid dermatitis. All had favorable evolution.

Conclusions: The prevalence of AR was similar to data described in the literature, despite the scarcity of studies in paediatric age.

The majority of AR were mild and did not required specific treatment, but often resulted on discontinuation of therapy.

From a preventive perspective, the existence of predictive factors of individual susceptibility to AR would be useful.

An awareness of the potential AR of therapies and a constant reassessment of the associated risks and benefits are required.
Objectives and Study: Highlighting associations of IBD with other disorders can facilitate understanding on the etiology of IBD and development of novel medications by exploring shared genetic pathways. In this nationwide study, we aimed to systematically explore the association of pediatric IBD with all other medical disorders in the history of all children diagnosed with IBD in Israel during the last 15 years compared with non-IBD controls.

Methods: This study utilized the validated nationwide epi-IIRN cohort that includes data from the four health maintenance organization (HMOs) covering 98% of the Israeli population. ICD9 codes of medical disorders were counted by the number of unique subjects (ever). A proportion test was used to assess the differences in rates of medical disorders between IBD patients and their controls. Bonferroni correction was used to adjust for multiple comparisons given the large number of evaluated disorders. Each PIBD case was matched to 2-3 non-IBD controls by sex, year of birth, district and HMO.

Results: A total of 5,240 children were diagnosed with IBD since 2005 and were included in the analysis (3,488 (66%) CD and 1,752 (33%) UC; mean age at diagnosis 13.5±3.6 and 2,348 (44.8%) females) matched to 13,827 controls. There were 283 different ICD9 codes related to 73 medical disorders recorded on the entire cohort. 30 (41%) disorders were very rare (<10 IBD patients) and other 24 (32.8%) were significantly different between CD patients and their matched controls (Table). In UC, 10 (13.6%) disorders were significantly different than their matched controls, all were also included in the CD list. Overall the disorders were grouped into allergic conditions, rheumatologic disorders, autoimmune and immune-mediated conditions, immunosuppressive disorders and others (including chronic kidney diseases). Of the 24 disorders, 5 (6.8%) were associated with IBD (i.e. extraintestinal manifestations and PSC).

Conclusions: In this nationwide study of all children with IBD in Israel, using a systematic analytic approach of all available diagnoses in the electronic medical charts, we found multiple medical disorders associated with PIBD. Some associations are well known but some were not hitherto recognized as IBD-related. Further studies are now needed to focus on each association for elucidating the nature of the association. Some of the associations may be treatment- or IBD-related and some may reflect more frequent health service utilization and thus more recorded diagnosis.
### Table: A list of 24 medical disorders significantly associated with CD and UC (n=5,240) vs. 13,827 matched non-IBD controls

<table>
<thead>
<tr>
<th>Label</th>
<th>CD</th>
<th>CD controls</th>
<th>OR (95%CI)</th>
<th>UC</th>
<th>UC controls</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allergic diseases</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Eosinophilic esophagitis</td>
<td>11</td>
<td>2 (0%)</td>
<td>14 (3-202)</td>
<td>5</td>
<td>0 (0%)</td>
<td>-</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>835</td>
<td>1731</td>
<td>332</td>
<td>5</td>
<td>332</td>
<td>-</td>
</tr>
<tr>
<td>Urticaria</td>
<td>1963</td>
<td>2167</td>
<td>510</td>
<td>5</td>
<td>510</td>
<td>1.3 (1.1-1.6)</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>2093</td>
<td>4172</td>
<td>862</td>
<td>6</td>
<td>862</td>
<td>1.4 (1.3-1.6)</td>
</tr>
<tr>
<td><strong>Immunodeficiencies</strong></td>
<td></td>
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<tr>
<td>Agammaglobulinemia</td>
<td>8</td>
<td>0 (0%)</td>
<td>2 (0%)</td>
<td>2</td>
<td>0 (0%)</td>
<td>-</td>
</tr>
<tr>
<td>Other immunodeficiencies</td>
<td>72</td>
<td>11 (0.1%)</td>
<td>17 (9.4-33.4)</td>
<td>6</td>
<td>6 (0.1%)</td>
<td>12.6 (5.3-31.1)</td>
</tr>
<tr>
<td><strong>Rheumatological disease</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td>21</td>
<td>7 (0.1%)</td>
<td>8 (3-18.8)</td>
<td>8</td>
<td>0 (0.1%)</td>
<td>21.1 (2.6-186.6)</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>54</td>
<td>0 (0%)</td>
<td>5 (0.3%)</td>
<td>5</td>
<td>0 (0%)</td>
<td>-</td>
</tr>
<tr>
<td>Juvenile idiopathic arthritis</td>
<td>40</td>
<td>1 (0.1%)</td>
<td>17 (7-42.4)</td>
<td>6</td>
<td>0 (0%)</td>
<td>15.8 (1.9-131.3)</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>15</td>
<td>3 (0.1%)</td>
<td>4 (0.3%)</td>
<td>4</td>
<td>0 (0%)</td>
<td>5.3 (1-21.7)</td>
</tr>
<tr>
<td><strong>Autoimmune diseases and related immunee</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>17</td>
<td>1 (0%)</td>
<td>45.2 (5.3-359.8)</td>
<td>22</td>
<td>1 (0.1%)</td>
<td>58.4 (7.9-433.8)</td>
</tr>
<tr>
<td>SLE</td>
<td>36</td>
<td>1 (0%)</td>
<td>58.3 (13.2-270.3)</td>
<td>64</td>
<td>0 (0%)</td>
<td>57.2 (14.3-270.3)</td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td>184</td>
<td>6 (0.1%)</td>
<td>57.1 (2.3-111.9)</td>
<td>37</td>
<td>2 (0.1%)</td>
<td>12.4 (5.8-26.6)</td>
</tr>
<tr>
<td>Pemphigus</td>
<td>650</td>
<td>1020</td>
<td>04 (0.1%)</td>
<td>04</td>
<td>1 (0%)</td>
<td>150 (5.8-26.6)</td>
</tr>
<tr>
<td>Lupus</td>
<td>39</td>
<td>1 (0.1%)</td>
<td>19 (1.7-2.1)</td>
<td>245</td>
<td>14 (1%)</td>
<td>1.3 (1.1-1.5)</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>30</td>
<td>5 (0.2%)</td>
<td>53 (2.9-9.9)</td>
<td>11</td>
<td>0.6%</td>
<td>3.6 (1.8-6.3)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>191</td>
<td>261 (2.8%)</td>
<td>50 (3.4%)</td>
<td>106</td>
<td>2 (3.3%)</td>
<td>1.5 (1-1.5)</td>
</tr>
<tr>
<td>Familial Mediterranean fever</td>
<td>68</td>
<td>57 (0.6%)</td>
<td>3.2 (2.2-4.9)</td>
<td>21</td>
<td>1.2%</td>
<td>1.8 (1.3-1.3)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>165</td>
<td>161 (2%)</td>
<td>1.6 (1.2-2.2)</td>
<td>32</td>
<td>2 (1.1%)</td>
<td>0.6 (0.3-1.3)</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>2156</td>
<td>4384</td>
<td>1065</td>
<td>230</td>
<td>3 (0.1%)</td>
<td>061 (52.8)</td>
</tr>
<tr>
<td>Autoimmune disorder</td>
<td>181</td>
<td>176 (1.9%)</td>
<td>2.8 (2.3-3.3)</td>
<td>81</td>
<td>4 (0.6%)</td>
<td>81 (1.9%)</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>12.4%</td>
<td>106%</td>
<td>4 (0.3%)</td>
<td>400</td>
<td>0 (0%)</td>
<td>1.1 (0.8-1.4)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>31</td>
<td>10 (0.2%)</td>
<td>5.2 (2.8-9.9)</td>
<td>14</td>
<td>0.8%</td>
<td>15 (0.3%)</td>
</tr>
<tr>
<td>Growth hormone deficiency</td>
<td>76</td>
<td>25 (0.3%)</td>
<td>3.8 (2.8-9.4)</td>
<td>10</td>
<td>0.6%</td>
<td>14 (0.3%)</td>
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</table>

Volume 3, Supplement 1, September 2022  173
Objectives and Study: Eight items were previously selected during stage-1 of the TUMMY-UC development, a patient reported outcome (PRO) for pediatric ulcerative colitis (UC), based on 79 concept elicitation interviews with guidance from the FDA and EMA. An observer reported outcome (ObsRO) version was determined to be required for children younger than 8 years. Here we report the results of stage 2, aimed at finalizing the included items, and stage 3 aimed at prospectively validating the index for its psychometric properties.

Methods: The structure and exact wording of the PRO and the ObsRO versions of the TUMMY-UC were determined by cognitive debriefing interviews with children and their caregivers. Weights were assigned to each item based on ranking of importance. Then, in a prospective multicenter study, children with UC between 2-18 years who either underwent colonoscopy or provided stool for calprotectin completed the TUMMY-UC during 4 consecutive days, as well as 7 and 21 days thereafter for evaluating reliability and responsiveness. Construct and discriminative validity were assessed by different measures of disease severity and quality of life (QOL).

Results: The exact wording of the TUMMY-UC was determined in an iterative process of cognitive interviews with 107 children with UC (age 11±4 years, 39% males, 54 (50%) in remission, 33 (31%) with moderate-severe disease). The PRO and ObsRO versions were formatted with identical structure to ensure conceptual equivalence for incorporating the scores from both age groups into one TUMMY-UC score. Then, in the validation study, 84 children were prospectively recruited (52 underwent colonoscopy and 32 provided stool for calprotectin; age 12.1±4.3 years, 48% males, 30 (36%) in remission, 21 (25%) with moderate-severe disease). There was excellent reliability in the repeated day assessments (ICC 0.90 (0.84-0.94); p<0.001) and after 1 week in those judged as unchanged (0.90 (0.81-0.95); p<0.001). The TUMMY-UC total score had moderate to strong correlations with all constructs of disease severity: r=0.70 with UC Endoscopic Index of Severity (UCEIS), r=0.63 with IMPACT QOL questionnaire, r=0.43 with calprotectin, r=0.80 with the PUCAI, r=0.75 with patient/caregiver global assessment (GA), r=0.46 with CRP, and r=-0.38 with albumin (all p<0.015). There was a slight superiority to combining TUMMY-UC scores of two consecutive days. The index had excellent discrimination of disease activity categories (figure 1) with a score<9 defining remission (Sen=93%, Spec=84%, AUROC=0.95 (95%CI 0.93-0.99)). The DTUMMY-UC showed high responsiveness and differentiated well between children who improved, worsened or remained unchanged by 21 days. The best cutoff of the TUMMY-UC change score to define response was a change of ≥10 points (AUROC 0.94 (95%CI 0.89-0.97)).
Conclusions: The TUMMY-UC, constructed from a PRO and ObsRO versions for children 8-18 and 2-7 years, respectively, and supported by the EMA, is a reliable, valid and responsive index which can be now used in clinical practice and as an outcome measure in clinical trials.
A novel partial enteral nutrition protocol is effective in inducing clinical and endoscopic remission in active paediatric Crohn’s disease

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Objectives and Study: Exclusive enteral nutrition (EEN) is a first-line treatment in active luminal paediatric Crohn’s disease (CD); however, patients often find it difficult to adhere to. To improve compliance, it is beneficial to allow patients to consume some whole food alongside the enteral formula. Recent studies have shown that partial enteral nutrition (PEN) could also be effective in inducing remission in active paediatric CD, especially when PEN is combined with a CD exclusion diet (CDED). The aim of our study was to determine clinical and endoscopic remission as well as mucosal healing in patients treated with a novel PEN treatment protocol (75% of daily dietary needs covered by polymeric formula, with one meal per day from CDED representing the remaining 25% of caloric intake) and to compare it to the standard EEN treatment protocol.

Methods: Patients in the PEN group were treated with a novel PEN protocol which allows one meal per day from CDED alongside the enteral formula. Our CDED was adopted to fit local cuisine. Patients in the EEN group were treated with the standard EEN protocol (100% dietary needs from a polymeric formula). All patients were assessed at weeks 0, 1, 3, and 6, using clinical and laboratory parameters. Endoscopic assessment was performed at induction and the end of treatment, at week 6.

Results: From June 2017 to the end of February 2021, 54 patients with active CD, treated in a single tertiary centre, were prospectively included in the study. Active CD was defined by Paediatric Crohn’s Disease Activity Index (PCDAI) > 10 and Simple Endoscopic Score for CD (SES-CD) > 3. Thirty-three patients were eligible for enteral nutrition therapy, fourteen of them were recruited in the PEN and nineteen in the EEN group. On intention to treat analysis, clinical remission (PCDAI < 10) was achieved in 11/14 (78.5%) and in 13/19 patients (68.4%) in PEN and EEN groups, respectively (p = 0.698). On per protocol analysis, 11/13 (84.6%) in the PEN group and 13/16 (81.3%) in the EEN group achieved clinical remission (p = 0.999). After 6 weeks of treatment, endoscopic remission (SES-CD ≤ 2) was found in 7/13 patients (53.8%) in the PEN group and in 8/16 (50.0%) patients in the EEN group (p = 0.999), while mucosal healing rates (SES-CD = 0) were achieved in 38.5% with PEN and 43.8% with EEN (p = 0.999) (Figure 1).
Figure 1. The rates of clinical remission on per protocol (PP) analysis and on intention to treat (ITT) analysis, endoscopic remission, and mucosal healing after 6-weeks of treatment with partial (PEN) or exclusive enteral nutrition (EEN) in children with active Crohn’s disease.

Conclusions: In our study, our novel PEN treatment protocol, allowing one meal per day from CDED, was comparable in effectiveness to standard EEN treatment in inducing clinical and endoscopic remission in pediatric patients with active CD. Our PEN protocol allows patients to consume one meal per day alongside the enteral nutrition formula, which positively impacts the patients’ quality of life. Larger randomized controlled studies are warranted to confirm the results of our study.
A systematic review on clinical outcomes in paediatric inflammatory bowel disease patients

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Objectives and Study: We aim to report on response and remission rates in paediatric inflammatory bowel disease (PIBD) by reviewing prospective cohorts and registries and comparing outcomes.

Methods: One reviewer (JVH) performed a systematic worldwide literature search in MEDLINE and EMBASE from inception until March 17, 2022. In addition, all publications of the ImproveCareNow registry were reviewed. Inclusion criteria were: prospective cohort studies with patients <18 years at diagnosis and minimum follow-up of 1 year mentioning disease phenotype and disease activity. Exclusion criteria were: (i) reporting disease activity only at diagnosis, (ii) retrospective cohort studies, (iii) full-text unavailable, (iv) outcome limited to steroid-free remission. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) checklist guidelines and Newcastle-Ottawa scale for prospective cohort studies were applied.

Results: The search yielded 395 records and 7 inclusions with sample sizes ranging from 33 to 390 patients (total population: 888). The median follow-up ranged from 1 to 5 years. Proportions between groups were compared using a chi-square test with significance level of 5%. Disease location is consistent with cohorts for Crohn’s disease (CD) (p=.004) but not for ulcerative colitis (UC) (p=.69). L4 was more frequent in the Belgian cohort (χ²=4). Primary outcome: proportions of disease activity differed at M0 and M12 (p<.00001) with more inactive (χ²=5.5) and less moderate-to-severe disease (χ²=23). Secondary outcome: proportions of disease activity, limited to BELCRO (Belgium), did not differ between 1, 2, 3 and 5 years (p=.94). After 5 years these proportions did differ significantly from baseline (M0) (p<.0001 for evolution).

Table 1: disease activity at start of the study (M0) and 1 year follow-up (M12). A: inactive disease; B: mild disease; C: moderate-to-severe disease. IBD-U: IBD type unclassified; NA: not available.

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<tbody>
<tr>
<td>Population, n</td>
<td>CD, 84</td>
<td>UC, 56 CD, 90 IBD-U, 7</td>
<td>UC, 124 CD, 266</td>
<td>UC, 4 CD, 26 IBD-U, 3</td>
<td>UC, 22 CD, 12 IBD-U, 2</td>
<td></td>
</tr>
</tbody>
</table>


Conclusions: Prospective reports on evolution of disease severity in PIBD are scarce. The European cohorts report a significant decrease in disease activity after 1 year with more inactive and less moderate-to-severe disease. Proportions of disease activity did not differ between 1 to 5 year follow-up in the Belgian cohort but did differ significantly from baseline (M0) after 5 years.

The authors declare no competing interests nor funding.
P-125

The use of nutrition as a therapeutic strategy in children and adolescents with Crohn’s disease in Belgium.

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Objectives and Study: Enteral nutrition (EN) is increasingly used for treating pediatric Crohn’s disease (CD). We retrospectively studied the use of EN in Belgium and to assess the effect of diet on disease activity and growth. The Belgian Society for Pediatric Gastroenterology and Nutrition (BESPGHAN) is currently implementing the Improve Care Now (ICN) registry for Belgian CD patients. The ICN registry collects clinical data at each outpatient visit, including nutritional and growth status and the use of EN.

Methods: The medical files of Belgian pediatric patients (<18 yrs old) diagnosed with CD and identified to be included in the newly implemented ICN registry were analyzed from 2015 to 2020 for disease classification, use of EN, growth delay and BMI. Eleven variables were selected from the dataset. The response variable was BMI (kg/m²). The predictor variables were Modulife program diet, exclusive enteral nutrition (EEN), any specific diet (milkfree, lactosefree, glutenfree, meat free, excluding processed foods, including supplements), dietician involved, treatment, age at diagnosis, disease location and behavior, growth delay. Statistical analysis was conducted using the SPSS software v.28. Pie plots with %, mean and SD were calculated for BMI. Independent samples t-tests were used to compare BMI based on variables with 2 groups or ANOVA for more than 2 groups. A p-value =< 0.05 was considered significant. Effect size was calculated for each variable as well as power analysis.

Results: Data were collected from the databases of UZ Brussel, ULB, UCL and CHC Liège during the period 2015 – 2020. The final dataset consisted of 124 patients (39.5%UZBrussel, 43.5% UCL and 17%CHC Liege). We found no association between disease location or behavior and BMI (p 0.566 & 0.864 respectively). Growth delay was significantly associated with BMI (p < 0.05). Patients not needing biological treatment had a statistically higher BMI (p-value < 0.001). A large proportion of patients (81%) received EEN but results showed no statistical significance between those who were exposed or not (p-value = 0.667 > 0.05). In contrast, the Modulife program led to a significantly better BMI (19.8 ± 3.8 vs. 17.5 ± 3.9 p= 0.004) and patients on any type of specific diet had a mean BMI 19.7 ± 3.9 compared to the others with BMI 17.3 ± 3.1 (p=0.005). Involving a dietician showed a trend for better mean BMI (20.1±3.9) compared to not (mean BMI 18.9±3.9).

Conclusions: Results indicate no relationship between using a diet and age, disease location, behavior or growth, indicating the lack of criteria for implementing nutritional therapy. However, the use of Modulife program or any specific diet were associated with improved BMI.
Enteral nutrition as primary therapy of pediatric inflammatory bowel disease in the usa

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Objectives and Study: Nutrition is increasingly utilized as a therapeutic intervention for pediatric inflammatory bowel disease (IBD). We sought to use data from a multicenter clinical IBD registry (the ImproveCareNow Network, ICN) to estimate the frequency of use of enteral nutrition as primary therapy in the USA.

Methods: We queried the ICN registry for data since its inception in 2007 until the present. ICN collects clinical data at each outpatient visit, including nutritional and growth status and the use of primary enteral therapy. At each visit patients nutritional and growth status is classified as either satisfactory, at risk or in failure based on specific criteria. (https://www.improvecarenow.org/resources_for_care_centers, Model IBD Care Guideline). The study population consisted of patients <18 yr old with a diagnosis of IBD who had a visit on or before 5/31/2021.

Results: There were 28,639 eligible patients, with ages <6yr, 717 patients (2.5%); 6-12 yr, 5009 (17.5%); and 12 to <18 yr 22,913 patients (80%). Patients had Crohn’s disease (17,893, 63%); ulcerative colitis (8,664, 30%); or indeterminate colitis (1,989, 7%); 93 had missing data. Nutritional and growth status at the last visit are shown in Table 1: 11.2% had or were at risk of nutritional failure, and 6.8% had or were at risk of growth failure. In contrast, only 5.3% (1,529) of patients had ever received enteral nutrition as primary therapy. For the 1,529 patients ever treated with primary enteral nutrition, the physician global assessment (PGA) at the visit before and at the visit where the patient was receiving primary enteral therapy was quiescent disease activity in 22%, mild in 38%, moderate in 34% and severe in 6%.

<table>
<thead>
<tr>
<th>Nutritional Status</th>
<th>Growth Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>Satisfactory</td>
<td>23,816</td>
</tr>
<tr>
<td>At risk</td>
<td>2,570</td>
</tr>
<tr>
<td>In failure</td>
<td>550</td>
</tr>
<tr>
<td>Not assessed</td>
<td>896</td>
</tr>
<tr>
<td>Missing data</td>
<td>807</td>
</tr>
</tbody>
</table>

Conclusions: Enteral nutrition was infrequently used as primary therapy in this cohort of US children with IBD from 2007 until 2021. We plan to compare these data with a European cohort to compare differences in practices as well as to determine if nutritional interventions are increasingly becoming part of patient care.
The effects of inflammatory bowel disease on caregivers: absenteeism and job presenteeism. A SEGHNPH multicenter study
(Spanish Society of Pediatric Gastroenterology, Hepatology and Nutrition)


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Objectives and Study: Pediatric inflammatory bowel disease (pIBD) impacts the physical, psychological, and socioeconomic functioning of patients and caregivers. However, work productivity and activity impairment are often poorly evaluated in this population. The aim was to assess the effects on work productivity in caregivers of patients with pIBD.

Methods: We performed a multicenter, observational, cross-sectional and descriptive study from February 2021 to February 2022. The Work Productivity and Activity Impairment Questionnaires for Crohn's disease and Ulcerative Colitis (WPAI-CD-Caregiver and WPAI-UC-Caregiver), with 6 items each, were translated and adapted for the Spanish population and subsequently completed by the participants. These questionnaires explore 4 aspects: absenteeism (failure to attend work by an employee who was thought to attend, excluding vacation periods, strikes and sick leave), presenteeism (understood as a phenomenon that revolves around the worker’s anxiety about losing their job and is influenced by a high level of stress that forces the individual to report to work when they are not able to do so), loss of productivity labor and impairment of daily activity due to pIBD. Demographic and clinical data and results of the questionnaires were collected using the REDCap platform and analyzed with SPSS.
Results: A total of 207 patients from 28 hospitals were included, 117 were male (56.5%), 138 with Crohn's disease, 65 with ulcerative colitis and 4 with IBD unclassified. The mean age at the time of completing the questionnaire was 14.2 ± 2.4 years and the time of evolution of the disease was 2.4 years (IQR 1.2-4.9). Amongst the 207 patients, 115 (55.5%) were in remission (PUCAI < 10 or wPCDAI < 12.5). Data from 310 parents (186 mothers and 124 fathers) were obtained. Up to 75.8% of the fathers and 67.2% of the mothers had a remunerated job at the time of completing the questionnaire. 62.8% of parents experienced absenteeism from work in the previous week with a median of 12.7% of lost hours (IQR 5-10); 69.1% recognized deterioration or impairment of productivity during the working day, with a decrease in productivity that week of 40% (IQR 20-60%). The percentage of affectation/global deterioration of the working life of the parent secondary to the illness of the child was 38% (IQR 20-67). The deterioration of the parent's ability to carry out daily tasks was 54.3%.

Conclusions: pIBD negatively impacts the work and daily sphere of their parents. Having 50% more forms from mothers may be related to the fact that they are the main caregivers of the patients. However, the employment rate of our sample corresponds to that of the population aged 20-64 published by the INE (The Spanish National Statistics Institute).
Health-related quality of life in a pediatric population affected by Inflammatory Bowel Disease. A SEGHNP multicenter study
(Spanish Society of Pediatric Gastroenterology, Hepatology and Nutrition)


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Objectives and Study: Pediatric inflammatory bowel disease (pIBD) impacts the physical, psychological, and socioeconomic functioning of patients and caregivers. However, health-related quality of life (HRQoL) is often poorly evaluated in this group of patients. The aim was to assess HRQoL using the validated IMPACT-III questionnaire in patients with pIBD.

Methods: We performed a multicenter, observational, cross-sectional and descriptive study on HRQoL in pediatric patients aged 10 to 18 with pIBD and their parents or guardians, from February 2021 to February 2022. The IMPACT III (0-100 scale) and IMPACT III-P (0-100 scale) questionnaires were translated and adapted for the Spanish population and subsequently completed by the participants. The questionnaires consist of 6 domains: bowel symptoms (7 items), systemic symptoms (3 items), emotional functioning (7 items), social functioning (12 items), body image (3 items), and treatment/interventions (3 items). Each item uses a 5-point Likert scale ranging from 1 to 5; higher scores indicate better HRQoL. The total score consisted of adding the answers to the 35 questions. The result was converted into a value between 0 and 100, being 100 the best score on the HRQoL questionnaire.

Demographic and clinical data and the results of the questionnaires were collected using the REDCap platform and analyzed with SPSS , considering associations with p<0.05 as statistically significant.
Results: A total of 207 patients from 28 hospitals were included, 117 were male (56.5%), 138 with Crohn's disease, 65 with ulcerative colitis and 4 with IBD unclassified. The mean age at the time of completing the questionnaire was 14.2 ± 2.4 years and the time of evolution of the disease was 2.4 years (IQR 1.2-4.9). Amongst the 207 participants, 202 IMPACT-III questionnaires and 298 IMPACT-III-P questionnaires were valid. The median IMPACT-III score was 77.1 (IQR 66.4-84.2) and the IMPACT-III-P was 75.7 (IQR 61.9-84.2), p=0.25. We observed no differences in the different domains of IMPACT-III and IMPACT-III-P. The correlation of IMPACT-III-P between parents was strong and significant r=0.787, p=0.0001 as well as between IMPACT-III and IMPACT-III-P, r=0.734, p=0.0001, being slightly higher when the mothers answered (r=0.742 vs r=0.705). Out of the 202 patients, 115 (56.9%) were in remission (PUCAI < 10 or wPCDAI < 12.5) and had a higher total IMPACT-III score and in domains fourth and sixth than the patients with activity.

Conclusions: In this cohort, HRQoL was lower in patients with higher disease activity. The correlation between IMPACT-III and IMPACT-III-P was significant. HRQoL was better in those patients in clinical remission.
Personalised Azithromycin+Metronidazole (PAZAZ), in combination with standard induction therapy, to achieve a faecal microbiome community structure and metagenome changes associated with sustained remission in paediatric Crohn’s Disease (CD): initial results of a pilot feasibility study

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Objectives and Study: Early relapse in paediatric Crohn’s disease (CD) is associated with more severe disease course. The microbiome may play a crucial role in disease development. We have previously shown that a Bayesian approach can predict clinical course in children with CD following the first year after diagnosis with high accuracy when ensuring samples were truly treatment-naïve. We hypothesize that directly targeting the microbiome in high-risk individuals will improve clinical response to standard of care (SOC) induction therapy in a subgroup of patients with a relapse-associated microbiome profile. We report on initial findings on feasibility of a multicentre pilot study on different continents with treatment allocation based on stool sample results at baseline determined in Canada for all participants.

Methods: This is a 52-week, multicentre, randomised, controlled, open-label, add-on pilot study to test the feasibility of a larger trial evaluating the efficacy of adjuvant antibiotic therapy in 20 paediatric patients with mild-to-moderate-CD (10<PCDAI≤37.5). SOC induction treatment consists of the Crohn’s Disease Exclusion Diet+Partial Enteral Nutrition (CDED+PEN). Relapse-associated microbiome signatures at week 0 are evaluated using 16S rRNA gene sequencing and a previously generated Bayesian predictive model from BioMiCo based on baseline stool sample results. Patients will be allocated to treatment groups (A1,A2,B,C) depending on their disease activity and relapse-associated microbiome at week 4 (table 1). Subjects in group A2 or C will receive a combination of azithromycin 7.5mg/kg for 5 days/week for 4 weeks and 3 days/week for another 4 weeks, along with metronidazole 20 mg/kg/day for 8 weeks. The purpose of this pilot trial is to assess feasibility of a multicentre trial on different continents with treatment allocation at week 4 based on stool sample results at baseline (16S rRNA sequencing at Dalhousie University, Canada). Primary outcomes will assess feasibility of treatment allocation and possible efficacy of add-on antibiotic treatment in children with high risk for relapse by assessing sustained remission (PCDAI≤10, no need for re-induction) at 52 weeks. Exploratory outcomes will include changes in PCDAI, inflammatory and microbiome markers and patient reported outcomes.

Results: As of May 17th 2022, 12 patients have been enrolled in The Netherlands. Baseline stool sample prediction results were available at week 4 in 11/12 patients. The one exception was due to a technical problem with the sequencing run, and final results became available at the end of week 4. Three out of 12 patients were predicted to be non-responders: one stopped CDED after 1 week due to persisting symptoms and declining to continue diet; two were not in remission at week 4 and were given additional antibiotics. One is now on week 6 and the other is now in sustained low-calprotectin remission after 26 weeks (with CDED+PEN phase 3 maintenance only).
### Disease activity at week 4 | Relapse-associated microbiome | Treatment group | SOC induction treatment | Study intervention
---|---|---|---|---
Remission | Yes | A1 | Crohn’s Disease Exclusion Diet | n.a.
| No | B | | Azithromycin + Metronidazole | n.a.
No remission | Yes / No | C | | Azithromycin + Metronidazole |

**Conclusions:** Initial results of our pilot study show that allocation at week 4 based on stool sample results obtained at baseline can be feasible. Future results of this pilot study will provide on distribution of relapse-associated microbiome, inform power calculation for a larger trial, and include possible efficacy of add-on antibiotic therapy.
Head-to-Head Pharmacokinetic Analysis of Infliximab Mono- vs Combination Therapy in Paediatric Crohn’s Disease

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Objectives and Study: Post hoc analysis of the SONIC trial found superior efficacy of standard dosing infliximab (IFX) combined with azathioprine (combo) compared to IFX monotherapy (mono) in adults with active CD, with more favourable pharmacokinetics (PK) on combo treatment (1). Currently, many paediatric centres are increasingly using mono IFX with proactive therapeutic drug monitoring (pTDM) to minimise toxicity risks associated with thiopurine use. The aim of this study was to evaluate whether combo has PK benefits over pTDM mono IFX.

Methods: This PK analysis included paediatric CD patients who had drug concentrations measured as part of two prospective studies. Combo patients received labeled IFX (5mg/kg at 0, 2, 6wks followed by every 8 wks) with immunomodulator (IMM) in the TISKids study (2). Mono patients received IFX in the observational REFINE study where pTDM was standard of care (3). Inclusion criteria for the PK analysis were a weighted Paediatric CD Activity Index (wPCDAI)>40, age 3-17 years and body weight (BW)>10kg at baseline. Combo trough level (TL) (Sanquin, ELISA) and mono TL (LabCorp, ECLIA) were assessed at week 6, 14 and 22 (dose 3, 4 and 5). ECLIA is a drug-tolerant assay for antibodies to IFX (ATI) detection while the Sanquin ELISA is drug-sensitive (ATI were tested if IFX <3 μg/mL). A population PK model was built using a combined dataset from both cohorts with nonlinear mixed effects modelling software using stepwise covariate modelling (objective function value >10.83, p<0.001). IFX clearance (CL), area under the concentration curve (AUC), TL and ATI were compared between the two groups using Wilcoxon Rank tests.

Results: The combined cohort consisted of 80 patients (64% combo) and 264 TL and 92 peak concentrations were obtained. At baseline, the mono group had a higher wPCDAI, more prednisone use and lower serum albumin (Table1). A 2-compartment PK model with a negative correlation between albumin and CL and positive correlations between BW, erythrocyte sedimentation rate (ESR) and CL as well as BW and V1 adequately described the observed concentration data. For a 65 kg patient, average CL and central volume of distribution (V1) were 0.39 L/d and 5.5 L, with corresponding interpatient variability of 31% and 28%. IMM use did not explain the interpatient variability in CL. There was higher CL during steroid use (most stopped by infusion-3), but there were no differences in CL or TLs at infusion-4 or 5 by steroid exposure. Moreover, there was no difference in median combo CL 0.29L/d (0.23-0.35) vs 0.30 (0.23-0.40) mono CL (p=0.45). There was also no significant difference between exposure (AUC) 75,876μg*h/ml (60,719-96,168) combo vs 75,518 (62,521-96,520; p=0.81) mono, infusion-4 TL 4.4μg/ml (2.3-7.7) vs 4.7(2.4- 8.5; p=0.77) and infusion-5 TL 5.6μg/ml (3.2-8.8) vs 4.8(1.8-9.6; p=0.41). While not a PK covariate of CL, 1 mono patient discontinued IFX due to ATI. No combo patients had ATI detected. There was no difference in change of wPCDAI over time.

Conclusions: This study suggests that there are no PK differences (TL and CL) between combo and pTDM mono therapy in newly IFX started paediatric CD patients, though steroids were initially used during IFX induction without IMM. As clinical outcomes and ATI were more difficult to compare due to heterogeneous study designs, head-to-head clinical trials of early optimised dosing vs combo therapy are needed to further assess efficacy.

References:
2. Jongsma et al. Gut 2022
### Table 1: Baseline characteristics of proactive TDM monotherapy vs labeled combination therapy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
<th>Mono</th>
<th>Combo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>80</td>
<td>29</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Age, years (median [IQR])</td>
<td>14.0 [11.0, 16.0]</td>
<td>12.8 [10.6, 14.8]</td>
<td>15.0 [12.0, 16.0]</td>
<td>0.066</td>
</tr>
<tr>
<td>Sex (F), (%)</td>
<td>42 (52.5)</td>
<td>15 (51.7)</td>
<td>27 (52.9)</td>
<td>1.000</td>
</tr>
<tr>
<td>Prednisone use n(%)</td>
<td>23 (28.7)</td>
<td>21 (72.4)</td>
<td>2 (3.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight-based starting dose IFX</td>
<td>5.2 [5.0, 6.1]</td>
<td>6.2 [5.3, 7.8]</td>
<td>5.1 [5.0, 5.3]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>wPCDAI (n=29 vs 50)</td>
<td>62.5 [50.0, 75.0]</td>
<td>70.0 [62.5, 80.0]</td>
<td>58.8 [47.5, 70.0]</td>
<td>0.003</td>
</tr>
<tr>
<td>Albumin, g/dl (median [IQR])</td>
<td>3.4 [2.8, 4.0]</td>
<td>2.9 [2.5, 3.3]</td>
<td>3.7 [3.3, 4.0]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESR, mm/hr (median [IQR])</td>
<td>30.0 [18.0, 47.0]</td>
<td>33.0 [10.0, 68.0]</td>
<td>30.0 [20.0, 47.0]</td>
<td>0.985</td>
</tr>
</tbody>
</table>

Numbers are No. (%) unless otherwise noted. IQR = interquartile range; TDM = Therapeutic drug monitoring; F=female; BMI=Body Mass Index; IFX= Infliximab, wPCDAI= weighted Pediatric Crohn Disease Activity Index; ESR=Erythrocyte Sedimentation Rate

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**Conflict of Interest:**

**S. Vuijk:** The TISKids study was supported by ZonMw (The Netherlands Organisation for Health Research and Development) under project number 113202001, Crocokids (a Dutch fundraising organization to support research on IBD in children), and an Investigator-Sponsored Research Award from Pfizer (Study ID WI213008).

**L. de Ridder:** Collaboration (such as involved in industry sponsored studies, investigator initiated study, consultancy) with Abbvie, Lilly, Takeda, Janssen and Pfizer. Grant from ZonMw, ECCO, Pfizer.
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Sex and sexuality in IBD - the pediatric gastroenterologists’ point of view

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Objectives and Study: Although sexual dysfunction (SD) and sexually transmitted infections (STI) are occasionally encountered in patients with inflammatory bowel disease (IBD), physicians may be embarrassed to discuss these issues. This is especially true in adolescent patients, where parents are active participants in clinic visits. In addition, data in the literature about SD in this age group is limited. Our aims were to assess pediatric gastroenterologists (PedGI) knowledge and common practice regarding sexual advice and STI in pediatric patients with IBD.

Methods: A questionnaire was sent to all registered PedGI in Israel, and included 24 questions addressing knowledge of sexual behavior, SD, receptive anal intercourse (RAI) and STI in pediatric patients with IBD.

Results: Overall, 52 physicians completed the questionnaire (27 males, 52%). Only 50% provided the correct answer regarding the mean age at which Israeli youth start practicing sexual activity, whereas none were correct regarding the mean age when RAI is practiced. Fifty eight percent rightfully stated that SD is equally distributed among males and females and 38% responded that it is equally prevalent among patients with Crohn’s and those with Ulcerative Colitis. The most quoted, incorrectly, risk factor for SD was perianal disease. Seventy five percent thought that providers should talk about sex with their patients, but only 19% actually do so, most often in response to a patient’s query. Ninety six percent felt they do not have enough knowledge about SD in IBD. Finally, only 2% routinely obtain bacterial swabs for STI in patients with refractory proctitis, although 15% encountered such a problem in clinic.

Conclusions: Sexuality and SD are not discussed routinely in the pediatric IBD clinics by the majority of PedGI. Providers should obtain more knowledge in the field, and proactively discuss these issues with teenagers with IBD.
Safety and Potential Efficacy of Escalating Dose of Ustekinumab in Paediatric Crohn’s Disease (the SPEED-UP study) - A Multicenter Study from the Paediatric IBD Porto Group of ESPGHAN


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Objectives and Study: Escalation of the ustekinumab (UST) maintenance dosage was effective in adults with Crohn’s disease (CD), but no data are available for children. We evaluated the effectiveness and safety of dose escalation of UST in pediatric CD.

Methods: This was a retrospective multicenter study from 25 centers affiliated with the IBD Interest and Porto groups of ESPGHAN. We included children with CD who initiated UST at a standard dosing and underwent either dose escalation to intervals shorter than 8 weeks or re-induction of UST due to active disease. Demographic, clinical, laboratory, endoscopic, imaging, and safety data were collected up to 6 months of follow-up.
Results: Sixty-nine children were included (median age 15.8 years, interquartile range 13.8-16.9) with median disease duration of 4.3 years (2.9-6.3). Most children were biologic (98.6%)- and immunomodulator (86.8%)- experienced, respectively. Clinical response and remission were observed at 3 months after UST escalation in 46 (67%) and 29 (42%) children, respectively. The strongest predictor for clinical remission was lower wPCDAI at escalation ($p=0.001$). The median C-reactive protein level decreased from 14 (3-28.03) to 5 (1.1-20.5) mg/L ($p=0.012$), and the fecal calprotectin level from 1100 (500-2300) to 515 (250-1469) mcg/g ($p=0.012$) 3 months post-escalation. Endoscopic and transmural healing were achieved in 3/19 (16%) and 2/15 (13%) patients, respectively. Eight patients (11.6%) discontinued therapy due to active disease. No serious adverse events were reported.

Conclusions: Two-thirds of children with active CD responded to dose escalation of UST. Milder disease activity may predict a favorable outcome following UST dose escalation.
Unpacking the different popular diets for paediatric Crohn’s Disease - concerns around nutritional adequacy


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Objectives and Study: The first line treatment for inducing remission in paediatric Crohn’s Disease (CD) is exclusive enteral nutrition (EEN), where a patient drinks a nutritionally complete formula exclusively for 6 to 12 weeks. Despite the effectiveness of EEN, some patients may experience challenges including taste fatigue, monotony, and a lack of social participation with meals. Given these challenges, patients may turn to popular or fad diets for managing their disease. These diets are often restrictive, eliminating a number of foods and exacerbating the risk of underlying nutrient deficiencies in this patient population.

Methods: These case studies involved a nutrient analysis of evidence-based and popular diets for CD, including Crohn’s Disease Exclusion Diet (CDED), CD-TREAT, Specific Carbohydrate Diet (SCD), IBD Anti-inflammatory Diet (IBD-AID), Autoimmune Protocol (AIP) Diet, Gut and Psychology Syndrome (GAPS) Diet, and low FODMAP. Four cases were selected with mild-moderate CD: 11-year-old and 16-year-old, both male and female. A nutrient analysis of sample menus of each diet was completed using Food Processor version of 11.6.0 by ESHA Research. Results were compared to age and gender specific Dietary Reference Intakes (DRIs), population-based dietary intake data, and Health Canada Dietary Guidelines.

Results: Data are presented for Case 1, 11-year-old male. Findings were comparable to other age and gender cases. As compared to Acceptable Macronutrient Distribution Ranges (AMDRs), there was a higher percentage of energy from fats and lower from carbohydrates for the SCD (% kcal, fat and carbohydrate respectively: 59%; 30%), IBD-AID (52%; 37%), AIP Diet (50%; 23%) and GAPS Diet (60%, 21%). Saturated fat intake exceeded recommendations (>10% of energy intake) for CDED (% kcal, 14%) CD Treat (17%), SCD (11%), AIP Diet (15%) and GAPS Diet (20%). Vitamin D and/or calcium intake were below the Recommended Dietary Allowance (RDA) for CDED (% RDA vitamin D and calcium, respectively: 89%; 86%), SCD (23%; 53%), AIP Diet (17%; 28%), low FODMAP Diet (4%, 96%) and GAPS Diet (calcium 58%). Adolescent females versus males between the ages of 14-18 years may be at greater risk of inadequate nutrient intake, given the general increase in nutrient requirements yet lower caloric needs.

Conclusions: Given the increase in awareness and interest in popular diets for Crohn’s disease, it is imperative that clinicians are aware of the risks of inadequate nutrient intake with restrictive diets.
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Development of Framework for Professional Practice (FPP) for nurses working in Inflammatory Bowel Disease in adult and paediatric care settings

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Objectives and Study: The Royal college of Nursing (RCN) Roles descriptives for Inflammatory Bowel Disease nurse specialists was published in 2007 and needed updating to reflect advances in IBD Nursing since its inception. The IBD Framework for Professional Practice (FPP) aims to clarify IBD Clinical Nurse Specialist (CNS) roles at different levels and to provide support for the development of roles in IBD nursing, including paediatrics, reducing variability in care and supporting career progression.

Methods: In 2021 a working party was convened comprising of nursing representatives from Crohns and Colitis UK, RCN Gastrointestinal forum, RCN IBD Nurses group (Paediatric and Adult) and representatives from IBDUK to update the IBD Nurse role descriptives document. Based on review of current nursing practice documents, an FPP model was agreed to guide the reader through the CNS role. Tri weekly meetings ensured momentum was maintained and each section of the FPP was reviewed by all authors. There was consensus amongst the working party that as the role of CNS is an advanced nursing practice, entry level should start at ‘Enhanced’ level as defined by Health Education England (Leary 2019) with progression towards ‘Advanced’ & ‘Consultant’ if appropriate for nurse and service. The RCN Pillars of advanced nursing practice; clinical practice, research, education, and leadership were used to develop the FPP. The patient journey was used to populate the required skills and knowledge for an Enhanced level nurse, with subsequent levels building on the previous. Vignettes of each level were developed to apply the FPP to clinical situations. Paediatric and Adult CNS’s and patient members of CCUK were invited to review and feedback on the draft FPP using online surveys.

Results: Feedback from 16 CNS’s demonstrated a perceived need for this document and all (100%) felt that it reflected their roles. There was concern about how current roles fit into the FPP as 25%(4) felt they may straddle 2 levels, therefore further explanation around this was added to provide clarity. The link to role band was queried by 19%(3) however the FPP was not designed to match nursing bands with the level of skill. Patient feedback highlighted several areas that needed clarification, such as requesting blood tests and accessibility to IBD services. These were incorporated and adapted accordingly within the document.

Conclusions: The IBD FPP describes knowledge and skills at enhanced, advanced and consultant levels across the four pillars of advanced practical - clinical practice, research, education and leadership, aiming to standardise and enhance the consistency of care patients with IBD receive as well as reflect the development of a CNS career pathway. It is expected that the roles will overlap as the skills of the CNS develop, their role and practice will be at different levels dependant on local needs and individual abilities, practice may incorporate elements of all 3 levels. If, and when, a nurse progresses through the levels of practice they retain the skills associated with earlier levels as this is not a linear process. There is no expectation that every CNS will, or should, develop to advanced or consultant level. Eliciting feedback from the nursing and patient community ensured the FPP meets the needs of those who it has been developed to support.
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The fibre fermentative capacity of the gut microbiota is diminished in children with Crohn’s disease and it is independent of disease activity or treatment with exclusive enteral nutrition.


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Objectives and Study: Induction of clinical remission with exclusive enteral nutrition (EEN), has been associated with accompanying changes in the concentration of short chain fatty acids (SCFA) (a biomarker of fibre fermentation) in faeces of children with Crohn’s disease (CD) (1). Here, we assessed the fibre fermentative capacity of the gut microbiota of children with active CD in vitro, before, during and after EEN and compared with healthy children.

Methods: 44 faecal samples from 14 children (female, n=7, age, median [Q1, Q3]: 14.1 [11.1, 15.1] years) with active CD were collected before, during (4 weeks) and at the end of EEN (8 weeks) and after food reintroduction (median [Q1, Q3]: 21 [16, 31] days post-EEN). All children had achieved clinical remission at the end of EEN (weighted Paediatric Crohn’s Disease Activity Index <12.5). A single faecal sample was collected from 11 healthy children (female, n=4, age, median [Q1, Q3]: 12.4 [9.6, 13.0] years). 24-hour in vitro batch fermentations were performed using 4 fibre substrates (pectin, high-resistant maize starch, wheat bran and a mixture of the three). Net production of SCFA was measured with gas chromatography.

Results: Compared to healthy children, the total production of SCFA was significantly lower in children with CD, for all 4 fibre substrates, and regardless of the study timepoint (Figure 1). Net production of SCFA remained unchanged during EEN and at food reintroduction, and for all fibre substrates (Figure 1). No significant association with levels of faecal calprotectin was observed at any of the timepoints. Acetate production was significantly lower in children with CD compared to healthy children for all fibre substrates except for resistant maize starch (Figure 1). Likewise, except for pectin, production of butyrate was significantly lower in children with CD than healthy controls (Figure 1). Production of propionate did not significantly differ between any of the groups.
Figure 1: Production of SCFA after 24-hour in vitro fermentation of faecal samples from patients with CD (before, during and after EEN) compared to healthy volunteers. Asterisks indicate significant differences. A: before EEN, B: 4-week EEN, C: 8 weeks-EEN, D: Food reintroduction, HC: Healthy controls.

Conclusions: Fibre fermentative capacity is independent of disease activity in patients with CD and remains lower compared to healthy controls. It might be unlikely that the mechanism of action of EEN is mediated by modulation of fibre fermenting bacteria.

References:

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ML: PhD studentship was funded by the Engineering and Physical Sciences Research Council and Nestle Health Science.
UZI is funded by NERC Independent Research Fellowship NE/L011956/1.
RH is supported by an NHS Research Scotland Career Researcher fellowship and has received speaker’s fees, travel support and consultancy fees from 4D pharma.
RKR: reports speaker’s fees, travel support, advisory boards: Nestle, AbBiVie, Celltrion & Pharmacosmos.
KG: reports personal fees from Nutricia, research grants and personal fees from Nestle Health Science, personal fees from Dr Falk, Abbott, Servier, Mylan, and Baxter. SM has no conflicts of interest to declare. The funding bodies had no impact on study design, analysis or conclusions reached.
YouTube as a source of Food, Diet-Related Items and Advisory Comments for the management of Inflammatory bowel disease

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Objectives and Study: The exact way diet is involved in inflammatory bowel disease (IBD) remains elusive. Therefore, patients often seek information beyond that received from health professionals. This study assessed the information on IBD nutrition management patients may receive online via the YouTube platform.

Methods: A YouTube search was performed on 02/06/2020. The keywords: “Food”, “Diet” and “Nutrition” were used in combination with “IBD”, “Ulcerative colitis (UC)” and “Crohn’s disease (CD)”. The first 200 eligible videos from each search were assessed for eligibility. Videos discussing any aspects of food or diet (Food, Diet-Related Items & Advisory Comments-FODRIACs) in the management of IBD were included. Videos discussing established nutritional therapies (i.e., exclusive enteral nutrition) were excluded. The perception of presenters towards each FODRIAC in the management of IBD was labelled as “positive”, “negative” or “neutral/intermediate”. The role of a FODRIAC in the management of IBD was categorised as “symptom management”, “gut inflammation”, “microbiome manipulation” and “non-IBD related”. Subgroup analysis was performed by video presenter (patients vs health professionals), type of IBD (CD vs UC). Presence or absence of scientific evidence supporting presenter’s claims was also recorded.

Results: 160 videos discussed 122 FODRIACs with regard to nutrition management of IBD. Patient videos received a higher number of likes (85 [35, 156]) than health professional videos (44 [16, 1440], p=0.01). Scientific evidence was cited in two patient videos (1%). Avocado, salmon, bananas, white bread and rice received proportionally the most positive comments (Figure 1). Low-fibre diets, white bread and bananas were associated with better symptom management and vegan diets, blueberries and curcumin were considered beneficial for gut inflammation. Fruits and prebiotics were associated with enhancement of the gut microbiome. Conversely, processed and high-fat foods, food additives, high-sugar foods, tomatoes and carbonated drinks were almost unanimously considered as harmful in IBD management (Figure 1). Corn, spicy foods and carbonated drinks were mainly associated with symptom exacerbation and processed, high-sugar foods and gluten with exacerbation of inflammation. Neutral claims were often made about fibre and vegetables. Videos supported by scientific evidence reported a lower number of negative claims for fibre (positive: 4, negative: 0) than videos which lacked evidence (positive: 7, negative: 20, p=0.01). Results did not significantly differ according to video presenter or type of IBD.
Figure 1. Top 40 FODRIACs with positive, negative, neutral mentions towards IBD management

Conclusions: We have identified food components which are perceived as beneficial or detrimental in IBD management based on YouTube presenters. More research in the role of diet in IBD is required to allow patients and health professionals to receive and provide evidence-based information, respectively.

Conflict of Interest: K Gkikas: PhD studentship was funded in partnership from the University of Glasgow and Nestle Health Science. UZI is funded by NERC Independent Research Fellowship NE/L011956/1. RH is supported by an NHS Research Scotland Career Researcher fellowship and has received speaker’s fees, travel support and consultancy fees from 4D pharma. RKR: reports speaker’s fees, travel support, advisory boards: Nestle, AbbVie, Celltrion & Pharmacosmos. KG: reports personal fees from Nutricia, research grants and personal fees from Nestle Health Science, personal fees from Dr Falk, Abbott, Servier, Mylan, and Baxter. SM and VS have no conflicts of interest to declare. The funding bodies had no impact on study design, analysis or conclusions reached.
Polymeric formulas are effective for induction of remission in paediatric Crohn’s disease: are all polymeric formulas equal?

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Objectives and Study: Exclusive enteral nutrition (EEN) is an important and well-established first line therapy for effective induction of remission in paediatric patients with Crohn’s disease (CD). Historically, literature on enteral formulas has focused on protein classification (elemental, semi-elemental and polymeric), and has shown all to have comparable efficacy for the induction of remission. With the emergence of research related to novel diet therapies for CD that are principled on the presence or absence of ingredients or additives thought to be either beneficial or detrimental to intestinal health, the same considerations have thus far, not been well-studied with formulas. Our aim was to examine the efficacy of a polymeric formula enriched with TGF-β at inducing clinical and biochemical remission in patients receiving EEN as compared with standard polymeric formulas without TGF-β and semi-elemental and elemental products (SE/E).

Methods: A single-centre, retrospective chart review (1985-present) of 237 patients (126 males and 72 females) who received EEN orally or via feeding tube for treatment of CD for a minimum of 4 weeks. Thirty-nine patients receiving concomitant pharmacological induction therapy were eliminated and 198 remaining patients, ranging from 2 to 17 years of age with a mean age of 12 years SD 2.8 and with varying disease severity (90 mild, 74 moderate, 34 severe) were divided into 3 groups, according to which formula they received: polymeric with TGF-β (TGF-β) (n=25), polymeric without TGF-β (polymeric) (n=109) and semi-elemental or elemental (SE/E) (n=60). Achievement of clinical remission was assessed by Physician Global Assessment (PGA). Biochemical remission was defined by normalization of any of three abnormal serum biomarkers (ESR >20 mm/hr., Albumin < 35 g/L, CRP > 5 mg/L) and Physician Global Assessment (PGA). Results were compared between groups using the Fisher exact test.

Results: Clinical and biochemical remission rates between the TGF-β group and the standard polymeric group without TGF-β were not statistically significant (p=0.57, p=0.33). Similarly, there was no significant difference between clinical or biochemical remission rates of the TGF-β compared with the SE/E group (p=0.31, p=0.5). Remission rates between feeding tube/oral delivery of formula were not statistically significant (p=1.00 and p=0.55 for clinical and biochemical remission, respectively).
Table 1. Results comparing disease severity, delivery and clinical and biochemical remission rates, by formula group.

<table>
<thead>
<tr>
<th>Group</th>
<th>Total</th>
<th>Polymeric with TGF-β</th>
<th>Polymeric</th>
<th>Semi-Elemental/Elemental</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>198</td>
<td>25</td>
<td>60</td>
<td>113</td>
</tr>
<tr>
<td>Disease severity (# of patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mild</td>
<td>86</td>
<td>7</td>
<td>30</td>
<td>53</td>
</tr>
<tr>
<td>moderate</td>
<td>72</td>
<td>13</td>
<td>21</td>
<td>40</td>
</tr>
<tr>
<td>severe</td>
<td>34</td>
<td>5</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Delivery method (# of patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>30</td>
<td>8</td>
<td>21</td>
<td>1</td>
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<tr>
<td>NG-159</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral + NG-9</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Oral + NG-14</td>
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<tr>
<td>Oral + NG-3</td>
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<td>Oral + NG-14</td>
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<tr>
<td>Oral + NG-2</td>
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<tr>
<td>Oral + NG-108</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral + NG-0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical remission achieved (PGA/PCDAI) (# patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>146/198</td>
<td>21/25</td>
<td>46/60</td>
<td>79/109</td>
<td></td>
</tr>
<tr>
<td>(73.7%)</td>
<td>(84%)</td>
<td>(76.6%)</td>
<td>(72.4%)</td>
<td></td>
</tr>
<tr>
<td>Biochemical remission achieved (# patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100/182</td>
<td>16/25</td>
<td>28/56</td>
<td>56/101</td>
<td></td>
</tr>
<tr>
<td>(54.9%)</td>
<td>(64%)</td>
<td>(50%)</td>
<td>(55.4%)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Polymeric formula enriched with TGF-β is at least as effective as standard polymeric, semi-elemental and elemental products in achieving clinical and biochemical remission in patients with CD when given exclusively. Studying the impact of formula composition on efficacy of nutritional therapies needs further evaluation. Efficacy is however best defined with endoscopic mucosal assessment or established surrogates such as faecal calprotectin, both of these were unavailable in our study. Future prospective studies should aim to overcome these limitations.
Transition readiness in adolescents with IBD: Translation and Validation of the Transition Readiness Assessment Questionnaire (TRAQ-NL)

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Objectives and Study: Transition from paediatric to adult care can be challenging for adolescents and young adults (AYA) with Inflammatory Bowel Disease (IBD). This study aimed to develop a Dutch version of the Transition Readiness Assessment Questionnaire (TRAQ), a generic tool to measure transition readiness, and verify its validity and reliability.

Methods: Following COSMIN methodology, we performed translation, back-translation, pretesting and validation of the final TRAQ-NL questionnaire. The TRAQ consists of 20 items divided into 5 sub-scales (Managing Medication, Appointment Keeping, Tracking Health Issues, Talking with Providers, Managing Daily Activities), and is self-administered by the AYA. The minimum score on every item is 1 and maximum score of 5 with a sumscore of 100.

For the translation the back to back methodology was used. RASCH analysis was used for structural validation, and hypothesis testing for construct validity. Overall internal consistency of the TRAQ-NL was assessed using Cronbach’s alpha coefficient. Reference scores were calculated using percentiles.

Results: A total of 250 TRAQ questionnaires were evaluated in 136 AYA’s with IBD (56% Crohn’s disease, 58% male, median age 17.5 years (range 15.67-20.38)).

Total mean score was 3.87 (range 1.45-5). The data of one outlier (AYA scoring very low, total mean score 1.45) was not used in order to have evenly distributed data (mean score range 2.25-5).

We defined transition readiness as moderate in patients with score between 25th-50th percentile (total mean score 3.375 - 3.9), adequate when scores in 50th -90th percentile (total mean score 3.91- 4.7) and excellent when score was above 90th percentile (sum score >4.7). Transition readiness was low when score was below 25th percentile (<3.375).

Reliability with Cronbach’s alpha was good (0.87). The TRAQ-NL discriminated well between different levels of knowledge, especially in de lower levels.

TRAQ scores increased in patients who repeatedly completed the TRAQ-NL during their transition period, in the ages 16-20 years. Younger patients, concomitant illness, less visits to the transition outpatient clinic and dependence on parents associated with significantly lower scores. Boys (versus girls) and AYA’s with disease acceptance issues had nearly significant lower scores. AYA’s with a higher VAS of independency and transfer readiness, as well as TRAQs done after transfer to adult care scored significantly higher.

Conclusions: The Dutch version of the Transition Readiness Assessment Questionnaire (TRAQ-NL) is a reliable and valid tool. TRAQ-NL can be used to detect gaps in transition readiness skills in AYA’s with IBD transitioning to adult healthcare. TRAQ is a generic questionnaire and can thus be used to evaluate transition readiness in Dutch patients with other chronic diseases.
A Review of the Psychological Needs of Patients with Inflammatory Bowel Disease within a Specialist Paediatric Gastroenterology Department

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Objectives and Study: The role of psychological support for patients and families with chronic health conditions such as Inflammatory Bowel Disease (IBD), varies in focus, nature and complexity. There is an intricate relationship between stress and the course of IBD symptoms, with increasing evidence that stress drives inflammation and triggers changes to the immune system. Additionally, adjustment to a chronic health condition, for both patients and families, can be a complicated process and can significantly impact psychological health and quality of life. Psychological interventions can play a key role in supporting positive adjustment to diagnoses, promoting positive family functioning and quality of life, improving coping with symptoms, as well as understanding and managing the impact of psychological factors on physical health. Patients with IBD form a significant proportion of referrals to the specialist gastroenterology-psychology service. A review of these referrals was undertaken to identify the key referral reasons and to understand the needs for psychological support amongst children and young people with IBD and their parents and families. It is vital for our service, with large demands on its resources, to understand this referral information in order to develop service provision to meet patient needs effectively and efficiently.

Methods: A review of referrals to our specialist gastroenterology-psychology service, between April 2021 and March 2022, was undertaken. A further analysis was conducted on those referrals for young people and their parents and families with a diagnosis of IBD; identifying patient demographic information and reason for referral for both outpatients and inpatients during this time period.

Results: Patients with a diagnosis of IBD accounted for 33% of our outpatient and 36% of our inpatient referrals during this year-long period. There were differences in reason for referral between outpatients and inpatients and between male and female patients. The most common reasons for outpatient psychological referral included: adjustment to diagnosis, treatment compliance and anxiety. Referrals were for patients ranging between the age of 3 and 17 years. The most common reasons for inpatient psychological support included: parental support, adjustment to diagnosis and low mood and spanned a similar range of ages to outpatients (2 to 17 years).

Conclusions: The results of this service review highlight the need to consider the ways in which psychological support can be provided in order to meet the patient needs amongst the IBD cohort most effectively and efficiently. In a service where there is significant demand on psychological resource, it is important to consider creative and innovative approaches to service delivery and waitlist management. Service development ideas are discussed (with consideration of the relevant literature) to inform next steps in ensuring excellent psychological care for IBD patients within the specialist gastroenterology service.
Association of paediatric inflammatory bowel disease and chronic recurrent multifocal osteomyelitis: Our experience


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Objectives and Study: Chronic recurrent multifocal osteomyelitis (CRMO) is a rare aseptic bone inflammation that can occur in association with inflammatory bowel disease (IBD) in pediatric patients. Our aim is to describe the experience of patients with this dual diagnosis in our pediatric tertiary care center.

Methods: Retrospective descriptive study of patients <18 years old diagnosed with IBD and CRMO by Jansson criteria in the last 10 years (2011-2021). Medical records of patients with dual diagnosis were reviewed and epidemiological, clinical characteristics and outcomes after treatment were analyzed.

Results: Five patients were identified, 2 ulcerative colitis (UC) and 3 Crohn's disease (CD), with dual diagnosis (median age: 9.9 years [IQR: 4.98-17.43 years]) and male predominance (3/5) were identified. Two of the patients (2/5) were first diagnosed with IBD and subsequently with CRMO (median time between both diagnoses: 1.69 years). In 2 patients the diagnosis was concomitant and the remaining patient was diagnosed with CRMO prior to IBD. At the moment of CRMO diagnosis, all patients had bone pain with multifocal lesions on total body MRI and 4/5 active IBD. One of the two patients previously diagnosed with IBD, was in clinical remission on comboterapy (adalimumab and mercaptopurine). Corticosteroids and bisphosphonates were added for CRMO treatment with good response. The other patient with UC and colectomy was treated with topical salicylates due to pouchitis and with methotrexate for active extraintestinal manifestations (uveitis and sacroileitis). At CRMO onset, was switched to adalimumab with worsening of digestive and rheumatological symptoms, requiring functionalisation, achieving remission. The two patients diagnosed simultaneously receive anti-TNF therapy (Adalimumab) together with methotrexate, and additionally with corticosteroids in one of them and bisphosphonates in the other, achieving both digestive and rheumatological clinical remission. The patient diagnosed with CRMO prior to IBD received treatment with nonsteroidal anti-inflammatory drugs and bisphosphonates. At the time of IBD debut, required intravenous corticosteroids and then switch to anti-TNF therapy (Infliximab) in combination with azathioprine. During the follow-up all the patients continue with anti-TNF therapy, sustaining clinical remission at the digestive level in 4/5 and rheumatological inactivity in all of them.

Conclusions: CRMO is a rare extraintestinal manifestation associated with IBD. In our series, the debut of CRMO was associated with digestive activity in most of the patients. Different therapeutic strategies were established at the time of dual diagnosis, being the anti-TNF therapy the most commonly used for sustain remission, both digestive and rheumatological in the pediatric population.
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Biologic treatment after liver transplantation

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Objectives and Study: Sclerosing cholangitis (SC) is a rare chronic cholestatic liver disease, with consequential fibrosis, without any known therapies that impact the progression of disease. The association with inflammatory bowel disease (IBD) well known, it has been suggested a pathogenic link between gut and biliary inflammation, however the activity of these disease varies independently. There is no evidence of safety and effectiveness of biologic treatments after liver transplantation due to SC in IBD.

Methods: The Ist Department of Pediatrics, Semmelweis University take care of three patients suffering from IBD after liver transplantation on biologic therapy.

Results: Our first patient received adalimumab treatment for Crohn’s disease five years after liver transplantation. After anti-TNF ineffectivity vedolizumab treatment started, she could reach mild disease activity and good liver function. In our next patient re-transplantation would be needed due to the recurrence of SC in graft, however ulcerative colitis is active, which is a known contraindication of the transplantation. To control inflammation, he received infliximab treatment, but toxic shock syndrome appeared. Colectomy should be planned for this patient. Our third patient received adalimumab treatment for ulcerative colitis in the first year after the second liver transplantation. Despite the clinical remission of ulcerative colitis, SC reactivated in the graft. Colectomy is a difficult therapeutic dilemma for a young female patient, so first we decided on vedolizumab treatment.

Conclusions: Controversial data are available in the literature on effective treatment for IBD, which could positively affect SC course. Biologic treatments are effective for treating IBD after liver transplantation, however we observed a serious adverse event.
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**Crohn’s disease in niemann–pick disease type C**


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**Objectives and Study:** Crohn’s disease (CD) has been reported in association with Niemann-Pick disease type C1 (NPC1), but few cases are reported and only one case series has been described. Although the pathogenesis is unclear, NPC1 mutation has shown to induce a defect in autophagy in vitro models. We report a case of a teenager who presented a CD four years after NPC1 diagnosis.

**Methods:** Case Report

**Results:** A 16-year-old boy diagnosed with NPC1 at the age of 12, who presented with one-year history of painful perianal polyp and intermittent diarrhea. Initially, diarrhea was associated to Miglustat treatment and the perianal polyp was treated with topical steroids without response requiring surgical resection. Histology showed fibroepithelial polyp with granulomatous inflammation and multinucleated giant cells. Afterwards, he presented with multiple painful skin tags, rectal bleeding and weight loss. Physical exam showed a normal abdominal exploration and inflamed skin tags, fissures and superficial ulcers of perianal area. Laboratory tests demonstrated elevation of inflammatory markers (C-reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR)), and low iron levels. Stool microbiological study was negative and Faecal Calprotectin (FC) was elevated (5646 mg/kg).

An eosophagosgastroduodenoscopy (EGD) and colonoscopy were performed, showing a normal terminal ileum with small ulcers in the ileocecal valve and multiple ulcers from cecum to sigmoid colon. EGD was normal. Histology was compatible with CD, without granulomas. Magnetic Resonance (MR) Enterography was normal and pelvic MR showed significant transmural thickening of the rectal wall, and a small superficial fistula.

Anti-TNF therapy with infliximab (IFX) at 5mg/kg in combination with azathioprine, and antibiotics (metronidazole and ciprofloxacin) were started with partial response. After receiving the third induction dose, he was admitted to hospital due to clinical worsening with fever, rectorrhagia and severe perianal pain requiring the use of opioids. COVID-19 was diagnosed and IFX levels were performed showing sub-therapeutic levels (0.4 ug/mL). An IFX intensified reinduction treatment was administrated achieving therapeutic levels and clinical remission later on. Currently, after 2 months on combotherapy with IFX at 10mg/kg every 4 weeks and azathioprine the patient is on sustained clinical and biological remission.

**Conclusions:** Patients with NPC1 who present perianal skin tags or gastrointestinal problems should be screened for inflammatory bowel disease (IBD) due to the association of both entities related to autophagy defect in those patients. NPC1 diagnosis precede the onset of IBD in most of the cases being colonic CD with perianal involvement the most common form of presentation. Anti-TNF and thiopurines treatment have been described effective in other similar cases, in our patient was successful for both luminal and perianal CD.
A novel mutation (c.311G>C;p.Trp104Ser) in the ARPC1B gene causing vasculitis, immunodeficiency and very early onset inflammatory bowel disease (VEOIBD) – red flags for reassessment

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Objectives and Study: Introduction: Several monogenic IBD disorders have been described so far and the use of next generation sequencing (NGS) plays a major role especially in the disorders of infantile or very early onset inflammatory bowel disease (VEOIBD). According to current guidelines, an immunologic workup and genetic testing is suggested in all children with VEOIBD. Sometimes a second look/ genetic analysis should be performed due to rapid developments in this field, having implications on specific treatment options in these patients (e.g. allogeneic hematopoietic stem cell transplantation).

We report a patient with infantile onset IBD, presenting with a novel syndrome of combined immunodeficiency, atopic eczema, inflammatory bowel disease and auto inflammation. The monogenic disorder is caused by a mutation in the gene encoding actin-related protein 2/3 complex subunit 1B (ARPC1B). Heterozygosity of Met694Val in the MEFV-gene (familial mediterranean fever) might be a disease modifying factor.

Methods: Case-Presentation

Results: In our patient a cow milk protein colitis had been diagnosed during infancy because of bloody diarrhea and atopic dermatitis. After the introduction of an amino acid base formula symptoms transiently disappeared. Because of a thrombocytopenic vasculitis and recurrent intestinal bleeding despite strict diet in the follow up a thorough workup including immunologic workup, endoscopy and genetic testing (NGS) were initiated. Remission of the pancolitis was induced and maintained with mesalazin. The NGS-panel only revealed heterozygosity for FMF (Familial Mediterranean Fever – M 694 V). However an additional treatment with colchicine was started. Due to recurrent infections, persisting thrombocytopenic vasculitis and recurrent episodes with bloody stools despite treatment a second genetic workup was initiated. A most probable pathogenic mutation in the gene encoding actin-related protein 2/3 complex subunit 1B (ARPC1B) could be detected, which is a key molecule driving the dynamics of the cytoskeleton. This novel syndrome is associated with a combined immune deficiency, thrombocytopenia, auto-inflammation and intestinal inflammation. To date, only few patients have been diagnosed worldwide so that treatment options have to be discussed individually.

Conclusions: This case of a new genetic disorder resulting from a mutation in the ARPC1B complex emphasizes, that investigations (including genetic analysis) in patients with early onset IBD should be reassessed, especially if there are red flag signs (e.g. age of IBD onset, Co-morbidity). Suspicion of monogenic IBD, a close and multi-disciplinary follow up in early IBD and the second genetic workup revealed this new and rare monogenic form of autoinflammatory disease including IBD having implications on specific treatment options, including hematopoietic stem cell transplantation.
Paradoxical cutaneous reactions to Anti TNF-α in paediatric patients with inflammatory bowel disease: Experience in our unit.

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Objectives and Study: Anti-TNF alpha are the most commonly biologic drugs used to treat paediatric Inflammatory Bowel Disease (PIBD). Although they are safe, paradoxical reactions (PR), mostly cutaneous, associated with their use have been reported. However, few data, particularly in paediatric patients, has been published until now.

The aim was to evaluate the incidence of paradoxical cutaneous reactions to anti-TNF in our cohort and to describe the demographic characteristics and the management of these patients.

Methods: Retrospective analysis of paediatric patients with IBD who developed cutaneous PR under treatment with anti-TNF during the last 15 years was performed. Demographic (gender, baseline disease and age at diagnosis), pharmacological (type of anti-TNF, dosage and time to develop adverse reaction) were analyzed. The main characteristics of PR (type, location, baseline disease status) and its medical treatment (type, modifications in anti-TNF treatment and evolution) were also assessed.

Results: We identified 121 patients on anti-TNF treatment, being adalimumab the most commonly used (70/121). A total of 13 cutaneous PR were found in 12 different patients, with a cumulative incidence (CI) of 10.7% (9 cases of paradoxical psoriasis, CI 7.4%, and 4 cases of hidradenitis suppurativa, CI 3.3%). Most of them (10/12) had Crohn’s disease and there were no remarkable difference in gender among these patients. The median age at IBD diagnosis was 9.5 years [IQR: 4.5] and the median time to develop PR was 28.5 months [IQR: 20.5], with most patients (11/12) on IBD clinical remission. Most of them (8/12) were on Adalimumab and all patients were in maintenance phase, although 5/12 were receiving an intensified regimen. In paradoxical psoriasis, the most frequent form was vulgaris, located mainly on the scalp and retroauricular area. In 10/12 the specific treatment of the PR was topical. In half of the patients (6/12) baseline treatment was modified due to poor control of IBD symptoms and/or presence of PR. The evolution of the PR was favourable in more than 80% of patients (10/12).

Conclusions: Paradoxical cutaneous reactions to anti-TNF is non negligible with an incidence of approximately 10%, being the paradoxical psoriasis the most frequent one, mainly located on the scalp and retroauricular area. Topical treatment is usually successful, although in torpid cases the cessation of anti-TNF drug and switch to a drug with different therapeutic target is needed. Our experience is similar to the one described in other series.
Severe refractory Crohn’s Disease with autoimmune hepatitis responsive to thalidomide

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Objectives and Study: Thalidomide is an effective immunomodulatory drug due to its inhibitory effects on TNFα, IFNϒ and IL12 together with its stimulatory activity on IL4 and IL5. Its efficacy in paediatric Crohn’s Disease (CD) has been reported in refractory CD patients, although further studies are required to confirm the generalizability of these findings. Known potential toxicity, such as sedation, neuropathy and teratogenicity, limits its use in paediatric age. Our aim is to describe a case of steroid-dependent CD with autoimmune hepatitis refractory to anti-TNFα (infliximab-IFX and adalimumab-ADA) and ustekinumab, in which remission of both intestinal and liver disease was obtained with thalidomide.

Methods: In July 2018 a 10-year-old boy presented onset of bloody diarrhoea (6-8 stools/day) associated with abdominal pain, nausea, weight loss and eczematous psoriasis. Ileocolonoscopy revealed serpiginous ulcers in ileocecal valve, cecum and ascending colon together with hyperemia and oedema in rectum and sigmoid colon; no abnormalities were seen in terminal ileum or in esophagogastroduodenoscopy. Colon biopsies showed signs of chronic inflammation in lamina propria and active inflammation with neutrophilic infiltration and crypt distortion. A CD diagnosis was made. An attempt with exclusive enteral nutrition failed due to patient non-adherence, therefore oral prednisolone associated with azathioprine was started, but for symptoms relapse on steroid tapering, then substituted with IFX. IFX was started at 5mg/kg with three induction doses over 6 weeks, followed by maintenance therapy every 8 weeks, with initial remission. After 5 months, due to clinical and biochemical relapse IFX was optimized at 10mg/kg every 4 weeks without success. A switch to ADA, using a standard induction and maintenance regimen, was attempted obtaining remission for 11 months. A subsequent symptoms relapse, unresponsive to ADA optimization (40mg every week), led to a new course of oral prednisolone together with CD specific diet with a transient 5-month remission. In February 2021 a new severe clinical relapse (4-5 loose stools/day, abdominal pain and fever) was associated with a first finding of increased liver enzymes (ALT 403 U/L, AST 91 U/L). Further hepatological assessments revealed ASMA positivity and at liver biopsy an interface hepatitis with plasma cell predominance in the portal inflammatory infiltrate; ANA, anti-LKM as well as hepatotropic viruses were negative. A new course of steroids and switch to ustekinumab were attempted with initial symptoms improvement and transaminases reduction.

Results: Due to continue relapses at steroid interruption, despite ustekinumab therapy, the latter was interrupted at the 4th dose. In July 2021, during the last relapse associated with transaminases increase, thalidomide was started (50mg/day). A dose optimization at 100mg/day after 7 days led to CD remission and liver normalization. After 5 months an altered sural nerve conduction assessed at the regularly scheduled neurophysiological follow-up led to reduction of thalidomide dose to 50mg/day with stable CD remission and without further nerve deterioration.

Conclusions: In our case thalidomide resulted as an effective treatment for severe refractory CD; however, potential neurotoxicity warrants regular neurophysiological monitoring.
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EBV positive mucocutaneous ulcer (EBVMCU) in pediatric Crohn’s disease - the Importance of pathology

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Objectives and Study: To Describe a unique case of EBV-positive mucocutaneous ulcer in a 17-year-old boy with ileocecal Crohn’s disease

Methods: case report

Results: A 17-year-old male, with ileocecal Crohn’s disease since age 12 years, underwent endoscopic evaluation for loss of response to infliximab (IFX) [7mg/kg q5weeks] and methotrexate (10mg per week) maintenance therapy. The IFX trough level was 17.05 mic/ml without anti-IFX antibodies. Colonoscopy and biopsies were normal except a large cecal ulcer (Figure 1a) the histology of which suggested a lymphoproliferative malignancy. PET/CT demonstrated a 5cm hypermetabolic process in the lower right abdomen, localized to the small intestine, with regional lymph node involvement. Ulcerated monoclonal EBV-positive B-cell lymphoproliferative disorder was diagnosed (Figure 1b-d). IFX and methotrexate were discontinued and surgical resection of the ulcer and the narrowed ileocecal valve was performed due to low suspicion for malignancy in setting of active Crohn disease. The surgical specimen indicated a solitary ileocecal ulcer with numerous EBV and Hodgkin’s-like cells. The cell morphology and immunophenotype, the circumscription of the base of the ulcerated aggregates, the numerous small T lymphocytes rimming the base, and the clinical context (Crohn’s disease) supported the diagnosis of EBV-positive mucocutaneous ulcer (MCU).

EBV-MCU, first described in 2010, can involve the oropharyngeal mucosa, skin, and gastrointestinal tract, primarily in the context of iatrogenic immunosuppression. EBV-MCU was included in the 2016 WHO classification of lymphoid neoplasms. This lymphoproliferative disorder with benign behavior often regresses spontaneously with reduced immunosuppression; however, local progression and systemic dissemination to lymphomas has been reported.

Five months’ post-surgery, our patient is in clinical and biochemical remission, on nutritional therapy with the Crohn’s Disease Exclusion Diet, without immunosuppressive therapy, under close follow-up with PET/CT every 6 months and scheduled for colonoscopy in one month.

Conclusions: Endoscopic evaluation with histopathological evaluation of biopsies is of crucial importance during exacerbation
Matched Unrelated Donor HSCT as curative modality for very early onset IBD caused by IL-10 RB defect

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Objectives and Study: IL-10 and IL-10 receptor defects are a cause of very early onset inflammatory bowel disease (VEOIBD). These patients are usually unresponsive to immunosuppressive therapies and haematopoietic stem cell transplant (HSCT) is a potentially curative treatment. Matched unrelated donor (MUD) HSCT has rarely been done for cure of the condition. Here we report the successful outcome in a 2 years old girl with IL-10 RB defect who underwent a MUD HSCT.

Methods: A female child born out of a non-consanguineous marriage had presented with recurrent infections, foul smelling discharge through the introitus and erythematous skin lesions in the groin folds since early infancy. She also had persistent diarrhoea. There were multiple perineal fistulae. The colonic biopsy revealed severe cryptitis with mucosal depletion. On investigating for a VEOIBD she was diagnosed on the clinical exome sequencing with a likely pathogenic homozygous IL 10 Receptor B mutation resulting in IBD-12 (chr21:g.33266466A>T; p.Met1?) . This was a novel mutation on chromosome 21 that alters the ATG start codon and consequently affects its translation. The child had to undergo a diversion ileostomy, due to the rectovaginal fistula. The child was planned for a matched unrelated donor HSCT.

She was admitted at 25 months of age for the HSCT. Conditioning regimen used consisted of busulfan, fludarabine and ATG. The child received a 10/10 HLA matched from a matched unrelated adult female donor with bone marrow stem cell product, at a dose of 5.6 million CD34+stem cells /kg . Cyclosporine was used for GVHD prophylaxis.

Results: Neutrophil and platelet engraftment post HSCT occurred on day +15. Post-transplant she had complications of a Staphylococcus aureus Hickmann tunnel infection and cytomegalovirus reactivation, which were successfully managed. The chimerism analysis on day+30 showed 100% donor cells indicative of a successful HSCT. She was discharged on day+46 after the HSCT. Presently she is more than 3 months post HSCT, with resolution of the fistulae and erythematous skin lesions over the groin. She is being transitioned to a normal diet with no further diarrhoea.

Conclusions: IL-10 and IL-10 receptor defects are a cause of very early onset inflammatory bowel disease (VEOIBD). We found a novel mutation in the IL-10 receptor B gene that resulted in the VEOIBD. After MUD HSCT the child had good short term outcomes.
Case report of a paediatric patient with chronic gastroduodenitis owing to 14q13.1q21.1 deletion


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Objectives and Study: To study the genotype-phenotype correlation and underlying molecular mechanisms of the rare NFKBIA gene variants. Interstitial deletions in chromosome 14q are rare. The resulting phenotype depends on the deletion size, breakpoints, and the genes deleted. The 14q13.1q21.1 region includes genes such as NKX2-1, PAX9, and NFKBIA. NFKBIA is associated with immunodeficiency and inflammatory bowel disease. However, because NFKBIA variants are rare, their genotype–phenotype correlation and underlying molecular mechanisms have not yet been elucidated. Herein, we present the case of a paediatric patient who underwent surgical intervention for severe duodenal stenosis caused by chronic gastroduodenitis since childhood who harboured a 14q13.1q21.1 deletion identified during genetic testing.

Methods: A detailed case report was prepared of a male paediatric patient suffering from chronic gastroduodenitis and has been subjected to array comparative genomic hybridisation to identify the genetic basis of the disorder.

Results: The boy suffered from gastro-oesophageal reflux disease since birth, and oesophagogastroduodenoscopy showed inflammatory cell infiltration from the corpus of the stomach to the second part of the duodenum. Subsequently, progression of gastric mucosal atrophy and ulcer formation in the duodenum leading to scarring were observed. Because duodenal stenosis occurred owing to scarring, surgical intervention was performed when the patient was 12 years old. Thereafter, chronic stomach and duodenum inflammation persisted, and several endoscopic balloon dilatations were performed to treat duodenal stenosis. Colonoscopy showed the prevalence of normal mucosa in the entire colon. The patient showed psychomotor delay, failure to thrive, and involuntary movements. Based on the features, a genetic disorder was hypothesised. Subsequently, array comparative genomic hybridisation was performed when the patient was 16 years old, which indicated a deletion of 14q13.1q21.1. Based on the genetic test results, corticosteroid therapy was started for the patient, to treat chronic gastroduodenitis.
Conclusions: NFKBIA variants can result in constitutive inhibitor activity and partial blocking of NF-kappa-B signalling. The signal plays a role in ectodermal development and alerts the innate immune system to the presence of pathogenic organisms. Patients harbouring the variants generally show phenotypes from infancy, including anhidrosis, dental abnormalities, sparse hair, failure to thrive, recurrent respiratory and gastrointestinal tract infections, and chronic diarrhoea. In our patient, no evidence of immunodeficiency and ectodermal dysplasia was found. Although NFKBIA variants have been reported to be associated with colitis in patients with inflammatory bowel disease, our case developed chronic gastroenteritis, not colitis. This case report suggests that genetic testing should be performed in children with atypical chronic gastroenteritis to investigate the involvement of immunodeficiency, even if the patient shows no signs of underlying immunodeficiency.
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Nutritional support of Ulcerative colitis case with 5-aminosalicylic acid (5-ASA) combined therapy

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Objectives and Study: Ulcerative colitis (UC) is a chronic inflammatory disorder of the gastrointestinal tract of unknown etiology common in the pediatric population. Many patterns of presentation are possible within the pediatric age group. The hallmark symptoms of UC include abdominal cramping, diarrhea, and bloody stools, but physical symptoms vary with extent, duration, and severity of the disease. UC affects the rectum, with contiguous involvement that can include the entire large intestine. There are several medical options for the induction and maintenance of disease remission, but the benefits of these medications need to be carefully weighed against the risks, especially in the pediatric population. Treatment of refractory ulcerative colitis (UC) is a common clinical challenge. In either acute or chronic refractory UC, the disease may continue to remain active, even though the patient is on an appropriate therapy.

Methods: We describe a case of pediatric ulcerative colitis with refractory to combined 5-aminosalicylic acid (5-ASA) therapy. A 4-year-old boy who presented with passage of loose bloody stool, abdominal pain, fatigue and erythema nodosum. Laboratory indicator: fecal calprotectine was noticeably elevated - 250 mkg/g. Diagnosis was confirmed by colonoscopy and histopathology.

Results: Treatment was thereafter begun with 5-aminosalicylic acid (5-ASA) oral. Initially, patient has clinical remission, but after a month, clinical signs again flared up. 5-aminosalicylic acid (5-ASA) suppository was introduced to treatment. The combined therapy with 5-aminosalicylic acid (5-ASA) was more effective than single oral dose. IBD MODULEN is a nutritionally complete formula that meets criteria for partial enteral nutrition as part of the Crohn’s disease (CD) has been added to the patient by mother’s wish. After adding this formula, the condition of the child noticeably improved. The patient was on clinical remission during 6 months. Nevertheless, 3 months later after introduction of MODULEN IBD, the patient has stopped receiving formula due to the lack of the formula in drug stores. The patient has started feeling abdominal pain, fatigue. After 6 months, he had bloody stool again, abdominal pain and fatigue. Colonoscopy showed that there was diffuse inflammation from the rectum to sigmoid colon, with some visible normal areas. Examination of the mucosa reveals a loss of the vascular pattern, high friability (hemorrhage when the endoscope rubs the colonic mucosa), and mucopurulent exudate (mucopus). The patient is now on refractory to high dose 5-aminosalicylic acid (5-ASA) combined therapy. The treatment option with corticosteroids is under consideration now.

Conclusions: The combined therapy of 5-aminosalicylic acid (5-ASA) oral and suppository was effective enough. Short term introduction of enteral nutrition Modulen IBD with 5-aminosalicylic acid (5-ASA) noticeably maintained clinical remission. Further investigations should be considered for detecting nutritional formula benefits on Ulcerative colitis flow.
An open study of outcomes in Paediatric Acute Severe Colitis and empiric use of PRASCO antibiotic cocktail

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Objectives and Study: Paediatric Acute Severe Ulcerative Colitis (P-ASUC) is a life-threatening gastroenterological emergency, predictive of poor long-term UC prognosis. Conventional medical therapy (CMT) has been limited to immunosuppression with intravenous (IV) steroids and Infliximab (IFX) including high and accelerated dosing IFX. High failure rates, with colectomy rates reported in up to 30%. There is interest in adjunctive therapy with the PRASCO oral antibiotic cocktail. We report our experience with PRASCO as rescue therapy for children with ASUC failing CMT.

Methods: Retrospective audit of children presenting to the Queensland Children’s Hospital (QCH) between January 2020 and February 2022 with P-ASUC and treated with PRASCO antibiotics as per Turner et al. after failing IV steroids and accelerated IFX. Data included PUCAI, CRP, platelets and albumin at presentation, day 0 and 5 of PRASCO therapy and at 3 and 12 months follow up. Colectomy rates were collated and categorised as acute (during admission) and delayed (post-discharge). Intestinal ultrasound (IUS) was performed during admission.

Results: 29 children presented to QCH with ASUC. 8 children (9 episodes) received PRASCO for colitis resistant to IV methylprednisolone and optimised IFX therapy, defined by PUCAI persistently >35. PRASCO was commenced on mean day 9 (range 3-16) of admission and after a mean of 6 days (range 4-16) IV methylprednisolone. 2 patients commenced PRASCO early (day 3 and day 5), had all been on maintenance IFX. The others had been on high-dose IFX for at least 4 days prior to commencement. 3/9 episodes did not respond to PRASCO and came to colectomy during the acute admission. In a further 3/9 episodes delayed colectomy was required (at a mean 4 months later), including one patient who initially responded to PRASCO but represented with ASUC and failed to respond to a second course. 3/9 patients sustained colectomy free periods at 18 months follow up. When grouped by outcomes (acute colectomy, delayed colectomy and no colectomy), improvements in PUCAI, CRP and albumin on D5 were noted in all groups, but CRP and albumin improved with greatest magnitude in the no colectomy group. PUCAI on day 1 of PRASCO was lowest in those who escaped colectomy. IUS was performed before (mean day of admission 2.2, range 1-6) and after PRASCO therapy (mean day of PRASCO 5.14, range 2-10) in 7/9 episodes. 5/7 had improvement in IUS after PRASCO defined by a reduction in extent of involvement, bowel wall thickening and/or vascularity. Those receiving PRASCO had more severe parameters at presentation than the 21 children with ASUC not treated: PUCAI 67.5 v 71.6, Albumin 29.8 (26-38) v 33.9 (20-43), CRP 30.8 (0.4-148) v 14.4 (0.4-64).

Conclusions: PRASCO resulted in improved PUCAI, albumin and CRP, and IUS in 8 children with severe ASUC resistant to maximal CMT and saved 3 from colectomy in the following 18 months. A further 3 had colectomy deferred, 2 for elective colectomy, 1 suffering a second ASUC episode. A lower PUCAI prior to PRASCO and improvement in D5 CRP and Albumin was predictive of those avoiding colectomy. The place of PRASCO in the management of P-ASUC warrants further evaluation.
An audit of Acute Severe Colitis outcomes in children in the modern era of accelerated Inflixi-mab (IFX)

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Objectives and Study: Presentation with Acute severe colitis (ASC) is associated with major short and long-term morbidities, including colectomy. Recent practice is more aggressive with biologics. We report our statewide experience of children presenting with ASC and practice of accelerated IFX (>10mg/kg in first 10 days vs 5mg/kg at 0, 2, 6 weeks) over the past 8 years, focusing on outcomes and prognostic indicators.

Methods: Chart review of children with ASC (PUCAI >65) January 2014 - April 2022 presenting to Queensland Children’s Hospital (QCH). Data on PUCAI, FC, CRP, Albumin was collected on days 0, 3, 5, 7 of admission, Infliximab use and hard outcomes at 3, 6 and 12 months of colectomy, recurrent ASC, sustained steroid/biologic free remission.

Results: 64 children presented with 83 episodes of ASC, median age 11.3 years (0.7-16); 26 males and were treated with intravenous methylprednisolone 1mg/kg. By day 7 steroids, 15/64 (23%) responded and did not require IFX. In the following 12 months, of these 15, 1 had colectomy for treatment refractory colitis, 5 recurrent ASC, 3 remained in steroid/biologic free remission, 2 commenced maintenance IFX, 2 needed further steroids and 2 lost to follow up. 49/64 (76%) received IFX for PUCAI >45 median Day 5. Dosing range was 10-40mg/kg in first 10 days, with total IFX dosing over first 4 weeks a mean 21mg/kg showing no change over the 8 years. By Day 3 IFX PUCAI improved to < 40 in 38/49 (78%). 2 did not respond to IFX and required acute colectomy on days 23 and 28. The remaining 9 had a PUCAI < 40 Day 7 of IFX. 14/49 (29%) who had IFX (9F:5M) had a second ASC episode within 12 months. Those with a recurrent ASC, had higher CRP (23 vs 18) and platelets (473 vs 426) respectively at presentation, with no predictive cut offs. In these 49, steroid free clinical remission (PUCAI <10) at 3, 6 and 12 months were: 63% (27/43); 52% (22/42); 47% (17/36) respectively. Cumulative colectomy rates at 3, 6 and 12 months were 3/43 (7%), 6/42 (14%), 10/36 (28%) respectively. Best Indicators for colectomy: CRP at presentation (60.4 vs 16.2), 72% coming to colectomy had CRP >25; male gender (7 vs 4), PUCAI Day 5 IFX (mean 34.1 vs 25.3). Overall for those presenting with ASC colectomy at 3, 6 and 12 months was 4/60 (7%), 7/54 (13%), 11/50 (22%) respectively. Neither PUCAI, FC, Albumin, BMI at presentation predicted response to steroids, colectomy nor repeat ASC. Higher CRP on presentation and PUCAI on Day 3 IFX best indicators for colectomy (mean CRP 60 v 16, PUCAI mean 44 vs 34). Children in steroid free remission at 12 months had lower CRP (Mean 25.7 vs 29.9) at presentation and lower PUCAI on Day 5 of IFX (19.3 vs 24.4).

Conclusions: In the modern era of ASC management using accelerated IFX, high rates of colectomy occur both acutely and within 1 year. Recurrent ASC is high within the first year. Those responding to IV steroids had a low colectomy rate but a low rate of 12-month steroid/biologic free remission. Best indicators of colectomy and 12 month sustained steroid/biologic free remission were PUCAI and CRP on Day 3-5 of IFX.
Infliximab Monotherapy for Treatment of Diffuse Enteritis Following Colectomy for Ulcerative Colitis in a 14 year old Boy

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Objectives and Study: To report rare entity of ulcerative colitis related severe enteritis (UCRSE) following colectomy in a child.

Ulcerative Colitis (UC) is an inflammatory bowel disease characterised by superficial diffuse mucosal inflammation involving the colon and rectum and follows a relapsing and remitting course. Small bowel involvement is limited to backwash ileitis. Colectomy is considered curative. The rare entity of UCRSE has been described primarily in the adult population. This condition appears to be triggered by colectomy in the majority of cases and is characterised by diffuse extensive enteritis with histology identical to UC. The mainstay of treatment is intravenous steroids in combination with an immunomodulator and in recent years anti–tumour necrosis factor agents.

Methods: Case report and literature review of UCRSE

Results: 14 yo boy was diagnosed with severe ulcerative pancolitis following presentation with a 3 month history of abdominal pain, bloody diarrhoea and weight loss. Treatment was initiated with intravenous methylprednisolone and escalated to infliximab (IFX) due to non response. Due to suboptimal response and frequent severe exacerbations, he had a trial of tacrolimus without improvement. At 5 months post UC diagnosis, he required an urgent subtotal colectomy for medically refractory acute severe colitis. Colectomy specimen and histology appearances confirmed the diagnosis of UC. Post operatively, he developed fevers, elevated inflammatory markers, severe abdominal pain requiring intravenous opioids and excessive stoma output up to 5000ml per day. Infective aetiology was excluded, Cross sectional imaging showed diffuse thickening of small bowel. With a high suspicion of UCRSE, gastroscopy and ileoscopy was performed 30 days post colectomy which revealed severe contiguous mucosal inflammation with ulcerations and spontaneous bleeding in the stomach, duodenum and illeum. Multiple biopsies demonstrated severe active chronic inflammation similar to ulcerative colitis lesions. He was commenced on 10 mg/kg of IFX rather than steroids due to concerns of wound dehiscence. Significant improvement was noted in both pain and stoma output within 72 hours post infliximab. He received 2 further doses of IFX in the next 3 weeks prior to discharge. He continues to be asymptomatic 4 months post colectomy on 8 weekly maintenance IFX monotherapy.

Of the 53 cases of UCRSE reported to date, only 3 were diagnosed under the age of 18. To our knowledge, this is the youngest patient with this rare complication following colectomy.

Conclusions: UCRSE following colectomy is an extremely rare condition in the paediatric age group leading to delayed diagnoses with associated significant morbidity. This case illustrates the need for consideration of UCRSE in a child with otherwise unexplained fever, severe abdominal pain and high stoma output post colectomy. IFX monotherapy is a successful treatment option.
Acute disseminated encephalomyelitis associated with very early onset IBD during infliximab therapy

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Objectives and Study: Infliximab (IFX) is a monoclonal antibody against tumor necrosis factor-α (TNFα) that plays an important role in the treatment of inflammatory bowel disease. However, previous reports revealed that TNF-α inhibitor preparations may increase the risk of infection and are associated with demyelination in the central nervous system (CNS) and peripheral neuropathy. This is a case of a very early onset inflammatory bowel disease (VEO-IBD) with acute disseminated encephalomyelitis (ADEM) during IFX treatment.

Methods: Case report

Results: The patient was a 9-year-old boy who presented with recurring periodic fever lasting for 1–3 days since infancy. He had been passing out bloody stools since the age of 2 years. Colonoscopy done at 3 years of age revealed edema and bleeding in the entire colon; hence, a diagnosis of VEO-IBD-like ulcerative colitis was made. Treatment with 5-aminosalicylic acid (5-ASA) was initiated, and the symptoms resolved quickly. He was treated with prednisolone (PSL) and 6-mercaptopurine (6-MP) due to relapse at the age of 4 years. However, 6-MP was discontinued because of elevation in the AST and ALT levels. In addition to PSL, a Chinese herbal medicine (natural indigo) was administered to maintain remission. At the age of 8 years, IFX was introduced due to unavailability of natural indigo. At 9 years of age, the patient presented again with fever and abdominal pain; hence, colonoscopy was performed, but no significant findings were observed. Computed tomography (CT) showed a contrast defect in the right kidney. The patient was diagnosed with acute focal bacterial nephritis (AFBN) and was treated with antibiotics. Four months later, there was a recurrence of fever and abdominal pain. Repeat CT showed contrast defect images of the bilateral kidneys, leading to a second diagnosis of AFBN. Voiding cystourethrography (VCUG) performed after treatment did not indicate vesicoureteral reflux (VUR).

Six months later, fever recurred which was accompanied with decreased consciousness and meningeal signs. The patient underwent magnetic resonance imaging (MRI) of the head, that showed multiple asymmetrical high-signal lesions in the deep and subcortical white matter on T2-weighted imaging, which was consistent with ADEM. Cerebrospinal fluid (CSF) findings showed pleocytosis, increased protein concentration and positive oligoclonal bands. Serum and/or CSF viral and autoimmune antibodies were negative. No pathological variants were found in any known IBD-related genes. Lymphocyte subset analysis, cytokine production studies, and cytokine profiles were performed to assess immune function; however, no significant results were obtained. The neurological symptoms improved after two courses of methylprednisolone (m-PSL) pulse therapy. IFX was discontinued due to the possibility of demyelinating disease caused by IFX. Since discontinuation, there was no relapse of ADEM.

Conclusions: ADEM has been reported as a rare side effect of IFX. The patient developed ADEM while maintaining remission with IFX. The mechanism underlying IFX-induced demyelination has not yet been elucidated. In VEO-IBD, where autoinflammation might be involved, the risk of developing ADEM with IFX may be increased; thus, caution should be exercised when prescribing IFX. This is the first report of VEO-IBD with ADEM during IFX therapy.
Hidradenitis suppurativa and Crohn’s disease: A challenging management

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Objectives and Study: Hidradenitis suppurativa (HS) is a chronic and inflammatory disease of the skin characterized by painful lesions in the apocrine gland areas of the body, most frequently in the axillary, inguinal and anogenital regions. In the literature a strong association between inflammatory bowel diseases (IBDs) and HS has been recognized. Common treatment options of HS include topical and systemic steroids, antibiotics and surgical drainage or resection. Anti-TNF agents have been shown to be effective not only in IBDs, but also in HS management, especially when patients are unresponsive to steroids or antibiotics. Nonetheless, after anti-TNF use, paradoxical reactions consisting in new onset or worsening of systemic or dermatological immune-mediated diseases have been reported.

Methods: Case presentation of a paediatric IBD patient affected by HS in the axillary region with a challenging management.

Results: A 12-year-old boy was diagnosed at our clinic with Crohn’s Disease (CD) with esophageal, duodenal ileo-colonic and perianal involvement and started on Infliximab (IFX) with clinical remission of gastrointestinal symptoms. However, one year later desquamative and essudative patches in the umbilical region, consistent with eczematoid psoriasis developed. Treatment with topical eosin solution and corticosteroid creams was performed and induced skin lesion resolution. Three years after the diagnosis CD flare up with diarrhea with mucus in the stool, increased fecal calprotectin and concomitant worsening of dermatitis was observed. Escalation of IFX treatment to 10 mg/kg per dose every 6 weeks was decided with resolution of both gastrointestinal symptoms and skin lesions. Unfortunately, six months later, abscesses in axillary region developed. The first one appeared in the right axillary region, it was initially treated with topical antibiotic therapy and subsequently surgically drained. One month later another abscess appeared in the left axilla, it was treated with systemic antibiotic therapy but only mild improvement. Therefore, the patient was diagnosed with HS, pathogenetically related to IBD, and IFX optimization every 4 weeks was decided. In the meanwhile, no further gastrointestinal flare up occurred. However, despite approximately 6 months from the IFX optimization with adequate trough levels, recurrent bilateral abscesses in the axillas have not completely resolve yet and the patient has shown frequent HS relapses that improve after local application of ozenoxacin. The patient was then started on doxycycline, but drug intolerance with abdominal pain and diarrhea was observed and the antibiotic therapy was discontinued.

Conclusions: Dermatologic manifestations in CD are a significant complicating feature that may exhibit a clinical course independent from gastro intestinal disease activity and be the result of paradoxical reactions to biological drugs. Specific therapeutic algorithms still remain undefined and pre-existing factors that can trigger paradoxical reactions to biological drugs have not been fully clarified yet. We report the case report of a 12 year-old boy with CD well controlled from the gastrointestinal point of view on IFX but with a difficult management of HS. Future research is needed to identify predictive factors and therefore to develop more effective treatment options.
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A possible association between new-onset blepharitis and anti-tumor necrosis factor therapy in patients with Crohn's disease: a case series.

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Objectives and Study: Anti-tumor necrosis factor alfa (TNFα) medications are the most frequently used biologicals to treat inflammatory bowel disease (IBD). Little is known about the ocular side effects of this drug category.

Methods: We present a case series of six young patients with Crohn's disease and no previous ophthalmologic manifestations who developed blepharitis after commencing treatment with anti-TNFα therapy.

Results: Six otherwise healthy patients with Crohn's disease, with no history of allergies or prior ocular complaints developed blepharitis at a median of 7.5 months after the initiation of anti-TNFα therapy. All ophthalmic findings were treated topically. The ocular symptoms of two of the patients resolved shortly after discontinuation of the anti-TNFα treatment. The other four suffered relapsing-remitting symptoms.

Conclusions: Blepharitis is a common ocular disease in the general population and an extra-intestinal manifestation in patients with IBD. It may be an adverse effect of anti TNFα therapy in the latter patient population.