

The Paediatric IBD Porto Group



ABSTRACTS

5th INTERNATIONAL SYMPOSIUM ON
PAEDIATRIC INFLAMMATORY BOWEL DISEASE

11 – 14 September 2019



Budapest Congress Center · Hungary

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Oral presentations

O-001

Effects of introduction of an inflammatory bowel disease nurse position on healthcare utilization

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Objective: Inflammatory bowel diseases (IBD) are chronic relapsing remitting diseases which potentially result in hospitalization, requiring long-term outpatient follow-up, ideally by a dedicated, multidisciplinary team. In this team, the IBD nurse is the key point of access for education, advice, and support.

The aim of this study was to assess the effects of introduction of an inflammatory bowel disease nurse position on healthcare utilisation.

Methods: An IBD nurse was instituted in September 2017 in our multidisciplinary IBD team. We compared differences in health care utilisation one year before (between 1st October and 30th September 2017) and one year after (between 1st October 2017 and 30th September 2018) the introduction of an IBD nurse position for all the patients with a confirmed diagnosis of IBD attending the Robert Debre hospital via 2 information sources PMSI and CEMARA.

Results: 252 patients (78.5% of the active file) were included in the patient education program. After the introduction of an IBD nurse position, fewer patients were hospitalized for a flare, with less hospital stays: 56 stays before versus 28 after, $p=0.002$. More patients were also hospitalized for diagnosis: 32 hospitalizations before versus 54 hospitalizations after, $p=0.001$. All other hospitalization categories were comparable, and the same reasons for hospitalization were found before and after (diagnosis, flare, planned colonoscopy, surgery, infection). Another interesting fact is the re-organization of the IBD team. The IBD patient education team was composed of an IBD doctor, the IBD nurse, the psychologist, the specialized dietician, and sometimes added by specialist pain team, and the adapted physical activity professor. 39 meetings gathered the team to share concerns about the patients and to improve the IBD health care system in the department: information brochures and booklets were designed, but also education materials (board games created for younger patients to allow them to understand their IBD). Moreover the entire diagnosis announcement pathway was redesigned to ensure a better integration.

Conclusion: This study demonstrates that the IBD nurse position reduces hospital admissions and clinic reviews. Instead of the traditional model, the IBD nurse provides accessible advice and allows patients to be outpatients.

O-002

Dietary intake and adherence to mediterranean diet in a cohort of pediatric patients with inflammatory Bowel diseases (IBD)

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Objectives and Study: Nutritional support is very important in the treatment of IBD children and includes the prevention of malnutrition and micronutrient deficiency and the promotion of optimal growth and development. Some patients believe that food induces or may exacerbate some symptoms such as abdominal pain and diarrhea; for this reason they modify their diet excluding foods like cereals, milk, vegetables and fruits, which are the main components of the Mediterranean diet (MD). The beneficial effects of MD can be attributed to the large consumption of antioxidants contained in fruits and vegetables and to a low consumption of saturated fats. The aim of the present study was to assess the dietary intakes of children with IBD in clinical remission in comparison with healthy controls in order to inform future dietary interventions. Additionally, we evaluated their adherence to the MD.

Methods: IBD pediatric patients in clinical remission and healthy pediatric controls were enrolled. The nutritional status was evaluated through a 3 day food diary, compiled by patients or parents. Adherence to the Mediterranean Diet was evaluated using a specific questionnaire, the KIDMED based on a test of 16 questions with scores ranging from 0 to 12 (> 8 optimal; 4-7 intermediate, ≤ 3 very low adherence).

Results: 100 IBD pediatric patients and 100 healthy pediatric controls were enrolled in the study. No differences in age, gender or ethnicity were recorded between patients and healthy controls. In IBD patients the median age at diagnosis was 14 years (range: 5-17), 52 were males (52%), 42 (42%) with Crohn's disease, and 58 (58%) with ulcerative colitis. The analysis of food diaries showed higher kilocalorie intake in patients with IBD compared to healthy controls (median: 1779 kcal vs 1602 respectively, $p < 0.001$) and an increase in carbohydrate intake (205 g vs 179 g, $p < 0.001$), including starch (138g vs 119g, $p = 0.003$), and in protein intake (69 g vs 62g, $p < 0.001$). Patients with IBD also had an increased intake of micronutrients and fibers. However, in the IBD cohort the score obtained by the KIDMED showed a level of adherence to MD optimal in 15%, intermediate in 40%, and low in 45%.

Conclusions: IBD patients have a sub-optimal food intake; however, most of them have an intermediate level of adherence to MD. This data raises questions concerning the food choices of children with IBD and can be used for future dietary interventions in this population, suggesting the need to encourage them to make better food choices more in line with the MD.

Clinical characteristics of Asian children with inflammatory bowel disease at diagnosis: data from a multi-centre Asian PIBD research network

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Objectives and Study: Paediatric inflammatory bowel disease (PIBD) is rising in incidence within Asia. There is a lack of pooled multi-centre epidemiological data on clinical disease characteristics in this population. The Asian PIBD Research registry was set up in 2017 to collate PIBD-related data across 11 paediatric gastroenterology centres in 7 Asian territories (Hong Kong, Malaysia, Philippines, Singapore, Sri Lanka, Taiwan and Thailand). We aim to present clinical characteristics of Asian PIBD patients at diagnosis from this inaugural collaborative effort.

Methods: Participating centres are responsible for registering all PIBD patients (< =19 years' age), and entering anonymized clinical data into a secure REDCAPS platform hosted by the Singapore Clinical Research Institute. Parameters examined at diagnosis were demographic parameters (age/gender/ethnicity), presenting symptoms, extra-intestinal manifestations, disease behaviour and phenotypic as per the Paris classification.

Results: Baseline data of 237 patients at diagnosis [Malaysia (n=58), Singapore (n=107), Taiwan (n=20), Thailand (n=36) and Philippines (n=16)] were analysed, phenotypically distributed as Crohn's Disease (CD) [59.1%, n=140], Ulcerative Colitis (UC) [36.3%, n=86] and IBD-Unclassified (4.2%, n=10). The majority of the cohort were male (61.2% n=145). In the multi-ethnic Malaysian/Singaporean PIBD cohorts, the Indian ethnicity was disproportionately over-represented (31.0-33.6%) relative to the respective country's population census (Indian 7.3-9.1%).

In this cohort, age of onset in 53.5% was less than 10 years with 28.8% very-early onset (VEO) [< 6 years] and 4.9% presenting below 2 years. UC patients presented at a significantly younger age than CD (mean age 7.4 vs 10.0 yrs, p< 0.001); 45.4% of VEO-IBD were UC versus 18.6% CD (p< 0.001). Compared with UC patients, CD patients were more likely to present with abdominal pain (60.0 vs. 41.9%, p=0.008), weight loss (59.3% v.s. 41.9%, p=0.011), fever (38.6% vs 11.6%, p< 0.001), anorexia (28.6% vs 9.3%, p=0.001) and malaise/fatigue (13.6% vs 4.7%, p=0.031). At diagnosis, CD patients had higher mean inflammatory indices: (ESR: 51.5 vs 39.5 mm/hr, p=0.01), (CRP: 58.8 vs 15.8 mg/L, p< 0.001) lower haemoglobin (10.5 vs 11.2 g/dl, p=0.04) and lower albumin (33.8 vs 36.6 g/L, p=0.028)

CD patients presented with predominantly ileocolonic (41.1%) disease with a relatively high proportion with perianal disease (26.0% v.s. 8.2% EUROKIDS¹). UC patients predominantly presented with E4-pancolonic disease (70.0%), followed by E2-left sided (16.2%) and E1-proctitis (10.0%).

Conclusions: We observed distinct epidemiological differences in our Asian IBD patients compared with prior published cohorts (Table); a younger age onset with proportionally more early-onset and very-early onset IBD, with a predilection for the Indian ethnicity. We also note a higher proportion of perianal disease amongst our CD patients. These distinct characteristics of the Asian PIBD patient warrant further research into possible differences in genetic and environmental etiologic factors.

References:

¹EUROKIDS Registry. *Inflamm Bowel Dis*, 2013.19(2):378-85.

²JCC 2017;11(2): 157-64.

³IBD 2013;19:423-28

Crohn's Disease	ASIAN PIBD (N=140)	EUROKIDS (N=1221)¹	Korean (N=594)²	China (N= 82)³
Mean age (range) yrs	9.98 (0.20 – 19.11)	12.5 (0.8 – 17.9)	15.0 (2 – 17)	9.9 (+/- 5.1)
A1a (< 10yrs)	62 (44.29%)	20.0%	2.4%	41.5%
A1b (10-17yrs)	71 (50.71%)	80.0%	73.7%	58.5%
A2 (17-40yrs)*	7 (5.0%)	/	23.9%	/
A3 (> 40yrs)	/	/	/	/

*A2 17-19 years (Upper limit of age in cohort is 19 years)

[Table : Comparing age of onset in CD patients with prior published cohorts]

The phenotypic spectrum of IBD in Canadian-born children of South Asian ethnicity: a prospective multi-centre comparative inception cohort study

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Objectives and Study: In Canada, where the incidence of paediatric Inflammatory Bowel Disease (9.6/10⁵) is among the highest worldwide, linkage of health administrative and immigration data indicates that first and second-generation children of South Asian ethnicity develop IBD at similar or higher rates to Caucasian youth. As a prelude to exploring genetic and environmental risk factors contributing to the heterogeneity of IBD, we compared the phenotypic spectrum of IBD in South Asian (SA) versus Caucasian children in a national inception cohort.

Methods: Patients aged < 17y presenting with new onset IBD at 12 participating academic paediatric IBD centres were enrolled from April 2014 in an inception cohort study of the Canadian Children Inflammatory Bowel Disease Network. Using standardised case report forms (CRFs), data were prospectively collected including patient demographics, ethnicity, baseline and longitudinal disease phenotypic features, treatments and clinical outcomes. Non-Jewish Caucasian and SA children were compared. SA was stratified into North SA (Punjabi, Gujarati, Pakistani, North Indian, Nepalese) and South SA (South Indian, Sri Lankan and Bangladeshi). Groups were compared using the Chi-square test or Mann-Whitney U test, as appropriate.

Results: Of 1259 children with new onset IBD enrolled between April 2014 and December 2018, 796 were non-Jewish Caucasian (98% born in Canada, 88% of parents born in Canada) and 118 SA (79% born in Canada, and 87% of parents born in SA). 5% of SA children had a first degree relative with IBD compared to 18% of Caucasians ($p < 0.001$). Major differences in demographics and phenotypic spectrum of IBD in SA versus Caucasian children are summarised in Table 1. Colon-only disease (UC/IBD-U or colon-only CD) predominated in SA, and CD overall was less common. The younger age of SA children at diagnosis was also observed in analysis restricted to UC/IBD-U (SA 11.6y (8, 14) vs Caucasian 13.6y (11, 15) ($p=0.02$)). At diagnosis weight loss (69% vs 49%, $p=0.006$) and iron deficiency anaemia (68% vs 47%, $p=0.008$) were more common in SA versus Caucasian UC/IBD-U. No differences were observed in the spectrum of disease severity at presentation, nor during follow-up. Anti-TNF exposure at 12 months was similar for SA versus Caucasian in UC/IBD-U (36% vs 41%, $p=0.49$), but lower for SA versus Caucasian with CD (43% versus 59%, $p=0.04$) despite an observed higher prevalence of perianal fistulising disease in the SA cohort ($p=0.05$). Whether anti-TNF exposed or naïve, over 2/3rd of children with CD and UC/IBD-U, had quiescent disease at 12 months regardless of ethnicity. Table 1: Baseli...

Conclusions: Although heterogeneous and encompassing a similar spectrum of disease severity in both populations, IBD in Canadian-born children of SA ethnicity differs from that observed in Caucasians, more commonly affecting the colon only, and for CD more commonly associated with perianal disease. Distinctive features of Southern versus Northern SA children, whilst intriguing, have been observed in a very small sample. Indeed, the early age of IBD onset and lack of family history in

SA children highlight the potential etiologic importance of early life exposures in the Canadian environment.

N (%) or median (IQR)	South Asian n=118	Caucasian n=796	p-value	North SA n=89	South SA n=25	p-value
Age (y)	11.5 (9.3, 14.3)	13.1 (10.8, 14.9)	0.03	11.3 (9.2, 14.3)	13.1 (10.9, 14.7)	0.17
Male (%)	62%	58%	0.42	56%	80%	0.03
Type of IBD CD; UC/IBD-U	48%; 52%	65%; 35%	<0.001	49%; 51%	48%; 52%	0.90
Colon-only IBD (CD-colon, UC, IBD-U)	67%	49%	<0.001	65%	74%	0.47
UC/ IBD-U extent E1;E2;E3/E4	7%; 9%; 84%	7%; 5%; 88%	0.21	7%; 7%; 86%	9%; 0%; 91%	0.81
CD Location (L1; L2; L3) any L4b disease	20%; 29%; 42% 24%	17%; 21%; 59% 28%	0.02 0.60	23%;27%;43% 30%	10%40%;30% 0%	0.40 0.09
Perianal fistulising disease	34%	17%	0.03	28%	60%	0.05
PGA mild; moderate; severe	UC:30%;39%;31% CD:23%; 38%; 39%	UC:28%;38%; 34% CD: 28%;48%; 25%	0.92 0.09	UC:27%; 42%; 31% CD:19%; 33%; 48%	UC:38%; 23%; 9% CD: 42% 50%; 8%	0.49 0.04
Endoscopic severity mild; moderate; severe	UC:18%; 47%; 35% CD:15%; 37%; 48%	UC:20%; 42%; 38% CD: 13%; 39%; 48%	0.74 0.91	UC:19%; 52%; 29% CD: 16%; 42%; 42%	UC:17%; 25%; 58% CD: 11%; 11%; 78%	0.16 0.12

[Table 1: Baseline demographic and phenotypic features of IBD]

Pro-inflammatory role of dietary fibers in IBD: defining how microbes shape the path to diet-associated inflammation, and guide diet-based therapies

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Objectives and Study: The etiology of inflammatory bowel diseases (IBD) remains unknown, although gut microorganisms and diet have been implicated. **Dietary fibers** pass through the bowel undigested, and are fermented within the intestine by **microbes**, typically promoting gut health. However, fiber receptors on immune cells are able to interact with fibers typically found on the surface of fungal cells, for example, resulting in a pro-inflammatory response. These fibers are structurally similar to dietary fibers, which many IBD patients describe experiencing sensitivity to. As altered balance between commensal and pathobiont microbes is a hallmark of IBD, we **hypothesized** that the loss of fiber fermenting-microbes populating the IBD gut leads to dietary fibers not being efficiently broken down to their beneficial byproducts (e.g., short chain fatty acids; SCFA), resulting in binding of intact fibers to host cell receptors. This can ultimately drive pro-inflammatory responses and a microenvironment that promotes continued dysbiosis and increased pathogenicity of select microbes, as observed in IBD.

Methods: Fiber receptor expression was examined using immunohistochemistry and flow cytometry of human biopsy tissues. ELISAs were utilised to evaluate cytokine secretion, in response to fiber (5mg/mL) or pre-fermented fibers, cultured with microbes of interest, in cell lines *in vitro* and biopsy tissues cultured *ex vivo*. Gas chromatography identified SCFA fermentation products.

Results: Presence of fiber receptors was increased in IBD biopsies. Whole-fibers induced pro-inflammatory cytokine production in macrophage, monocytes, and neutrophils. Specific microbes were capable of fermenting fiber into SCFA. Pre-fermentation of fibers by these microbes reduced inflammatory marker production. The fiber oligofructose increased IL-1 β in pediatric CD (n=26) and UC (n=21) biopsies cultured *ex vivo* but not in non-IBD (n=11). The increase was greater in patients with more severe disease. Pre-fermentation of oligofructose reduced this secretion of IL-1 β . Whole-microbe intestinal washes from severe IBD patients were unable to ferment oligofructose or reduce fiber-associated inflammation in macrophage cells compared to remission or non-IBD children. Statistical analysis of food frequency questionnaire (FFQ) data on fiber consumption demonstrated that fiber-associated inflammation in patient biopsies cultured *ex vivo* (ELISA and qPCR) correlated with fiber avoidance (FFQ).

Conclusion: Our results suggest an augmented sensitivity to unfermented fibers in IBD, by increased fiber receptors. Furthermore, more severe patients displayed increased inflammatory response to dietary fibers modulated by select immune cells. This can be prevented by allowing pre-fermentation by appropriate microbes, which are missing in intestinal wash samples cultured from severe IBD patients. Comparing *in vitro* findings to our readily available patient FFQs, intestinal washes (microbe abundance), and detailed patient history will better define the relationship between microbes, dietary fibers, and gut inflammation in IBD. These data will allow us to provide tailored dietary intervention to patients most likely to respond through the use of dietary recommendations, including microbe-altering treatments, such as prebiotic and probiotic therapies.

Fecal Short Chain Fatty Acids (SCFA) measurement and microbiome metatype shifts in nutritional therapy of paediatric Crohn's disease

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Objectives and Study: A recently completed randomized controlled trial (RCT) showed improved sustained remission with the Crohn's Disease Exclusion Diet + Partial Enteral Nutrition (CDED+PEN) as compared with Exclusive Enteral Nutrition (EEN)¹. Whole metagenome analysis and fecal SCFA were examined in CD patients reaching remission after 6 weeks of nutritional therapy.

Methods: Whole shotgun sequence data from stool samples were obtained from 53 patients at weeks 0, 6 and 12. Stool SCFA analysis was available for 128 samples (48 patients). Mann-Whitney U (for unpaired) - Wilcoxon signed rank (for paired samples) were used for SCFA measurements at different time points.

146 CD samples were combined with 26 healthy controls (HC)², and characterized using HUMAnN2. Reactions, substrates and products for genes with an enzymatic commission were input to an unsupervised Bayesian analysis of community metabolism (BiomeNet). Statistical analysis of community metabolism and SCFA concentrations were performed using R. Non-negative matrix factorization (NMF) and Structural topic models (STM) were used to identify patient-associated microbial metatypes.

Results: Unsupervised analyses revealed two metatypes. All HC possessed one metatype (M1). CD patients had a mixture of two metatypes (M1 & M2), with mixtures related to stage of treatment. CD patients achieving remission showed a steady increase in the M1 contribution as nutritional therapy progressed.

Fecal SCFA concentrations did not change significantly across the 3 timepoints in CDED+PEN, but there was a significant drop in butyrate in the EEN group vs. CDED+PEN at week 6 ($p=0.00028$). However, SCFA concentrations were associated with M1 and M2 mixtures in patients. M1 was associated with higher concentrations in butyrate ($p=0.012$), valerate ($p=1.2e-6$) and iso-butyrate ($p=0.008$). Genes involved in the 4-aminobutyrate, and crotonoyl-CoA to butyrate pathways, ($p=0.03$ to 0.0001) were associated with M1 and a different pattern of associated genes was identified in M2. Changes in fecal SCFA concentrations, though associated with M1, were not associated with clinical remission at week 6 in CDED+PEN. In EEN, there was a significant drop between week 0 and week 6 in butyrate concentration (Mann-Whitney $p=0.0018$, Wilcoxon signed rank $p=0.0046$).

The butyrate-related change in community function is attributable to shifts in bacterial species abundance, notably Bacteroides and Clostridium.

Conclusion: Diet-induced remission samples were associated with a metatype that characterized healthy controls and genes involved in the 4-aminobutyrate pathway, and crotonoyl-CoA to butyrate pathway. Although the higher concentrations of butyrate and other SCFA, associated with M1, agree with past work suggesting that butyrate levels are associated with reduced inflammation, we did not measure an increase in fecal butyrate in CDED+PEN. Conversely, remission achieved with EEN is associated with a decrease in butyrate at week 6. An expansion of Firmicutes and decrease in Proteobacteria was observed in both diets by week 6. This suggests that other metabolic processes are important in the microbiome community function shift associated with achieving remission.

References:

1. Levine A et al. Gastroenterology 2019.
2. Lewis JD et al. Cell Host Microbe 2017.

Severe pediatric Ulcerative colitis is associated with decreased Infliximab post-induction trough levels and poor disease outcomes

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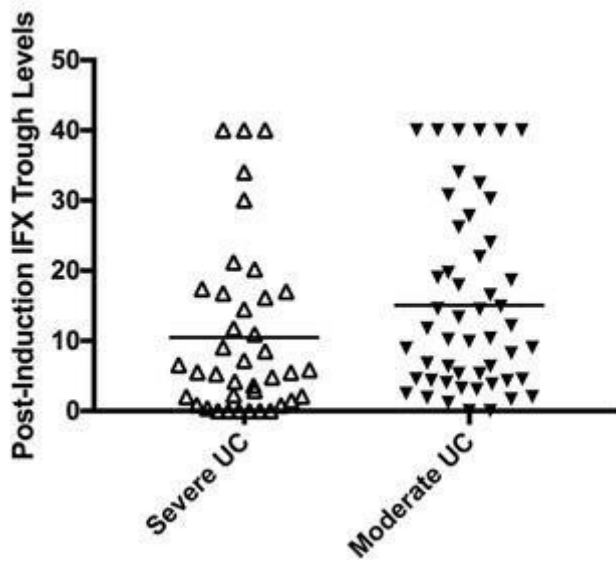
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Objectives and Study: The aims were to compare post-induction Infliximab (IFX) trough levels (TL) of severe Ulcerative Colitis (UC) versus moderate UC children and to evaluate disease outcomes, including primary non response (PNR), loss of response (LOR) at 12 months and colectomy rate at 24 months.

Methods: This was a single-center, retrospective study involving the IBD unit of the Children Hospital of Philadelphia. Children aged from 6 to 21 years with a confirmed diagnosis of UC, starting IFX with a PUCAI \geq 35 and with available post-induction TL between August 2012 and June 2018 were recruited. The following information were recorded: age at diagnosis; disease extent and clinical activity index before IFX starting; therapeutic history, IFX dosage, timing between infusions, PNR, LOR and surgery after IFX starting. Post induction TL and laboratory evaluations including complete blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and albumin at the moment of IFX starting were also collected.

Results: Ninety children were included in the analysis (median age at IFX starting: 14.5 yrs; range 6.4-21.2; M/F: 45/45). On the basis of PUCAI score, 39 (43.3%) were classified as severe UC (PUCAI \geq 65), while 51 (56.6%) resulted to be affected by moderate UC (PUCAI \geq 35 < 65). Median disease duration before IFX starting was significantly lower in ASC group when compared with moderate UC (p=0.01). Patients affected by ASC presented significant decreased mean values of hemoglobin (p=0.01) and albumin (p=0.001), while showing significant higher mean values of CRP (p=0.03) respect to patients with moderate UC. ESR was also increased with a trend towards statistical significance (p=0.07). No significant differences were identified in terms of concomitant therapies. A higher number of children with severe UC started IFX with a dosage of 10 mg/kg when compared with patients with moderate UC [26/39 (66.7%) vs 23/51 (45.1%); p=0.05]. Mean IFX post-induction TL were significantly lower in children with severe UC when compared to moderate UC (10.4 \pm 12 vs 15.1 \pm 12.9; p=0.03) (Figure 1). In details, 14 out of 39 (36.8%) children with severe UC had IFX TL \leq 3 compared with 7/51 (13.7%) children with a moderate disease activity (p=0.02). Antibody-to-IFX formation rate did not differ between the two groups after the induction. IFX post-induction TL were inversely correlated with CRP (r=-0.398, p< 0.001) and ESR (r=-0.330, p=0.01). Differently, IFX levels were positively correlated with hemoglobin (r=0.310, p=0.004) and albumin (r=0.358, p< 0.001). PNR did not differ when comparing severe and moderate UC children [3/39(7.7%) vs 7/51 (13.7%); p=0.5]. At 12 months of follow-up, 15 out of 39 (38.6%) ASC children interrupted IFX therapy for LOR versus 11/40 (21.6%) children with moderate UC (p=0.05). The 2-year cumulative colectomy rate was 15.38% (95% confidence interval (CI)=8.1-15.6%) in children with severe UC and 3.92% (95% CI=2.9-10.8%) in patients with moderate UC with a trend towards statistical significance (logrank test p=0.06).

Conclusion: These results demonstrated that children with a PUCAI \geq 65 at IFX starting present lower post-induction trough levels and more severe disease outcomes including LOR and a higher risk of surgery.



[Post-induction trough levels in children with severe or moderate UC]

Paediatric ulcerative colitis patients account for only 2% of total colectomy cases within a defined Scottish health board

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Objectives and Study: Paediatric-onset ulcerative colitis (UC; diagnosed < 17 years of age) is known to be more extensive than adult-onset disease with higher requirements for both hospitalisation and colectomy. However, few all-ages population based studies exist to determine the proportion of colectomies performed on children. We conducted an extensive multi-parameter search strategy to identify all cases of UC, and those requiring colectomy, within NHS Lothian (population = 897,770), a defined UK health board and the largest of three within South-East Scotland. We aimed to provide a robust estimate for colectomy rates in patients with UC and determine the true proportion of paediatric cases.

Methods: All prevalent patients with a diagnosis of UC between 01.01.05 - 31.12.2018 were extracted from the manually validated, multi-source population-based Lothian Inflammatory Bowel Disease Registry (LIBDR). We then identified patients who underwent colectomy using capture-recapture sampling from multiple clinical and administrative databases: NHS Lothian pathology database; NHS Lothian operating room scheduling database (ORSOS); NHS Lothian IBD multi-disciplinary meeting database; Information Services Division (ISD) inpatient coding database and South-East Scotland prospective PIBD database. All cases were manually validated by an IBD physician as per Lennard-Jones or revised Porto criteria; A1 age phenotype (< 17yrs at diagnosis) was determined as per Montreal and Paris classifications.

Results: A total of 447 patients underwent colectomy over the study period with 34/447 (7.6%) A1 phenotype. Colectomy rates per 100 UC patients fell from 1.49 (95% CI 1.02-2.10) in 2005 to 0.44 (95% CI 0.26-0.70) in 2018 ($p < 0.001$). The colectomy rate annual percentage change (APC) was -4.1% per year from 2005-2014 and -18.9% from 2014-2018 ($p = 0.019$). Rates of maintenance biologic therapy increased significantly over the same period; APC 11.2% from 2005-2012, 126.6% from 2012-2015 and 14.2% from 2015-2018 ($p = 0.022$). Only 10/447 (2.2%) colectomies were performed on children < 17 years of age. Median (IQR) age at colectomy 13.1 (12.5-14.9) years; 5/10 (50%) male; 7/10 (70%) received biologics. All 10 (100%) paediatric procedures were sub-total colectomies performed by an adult colorectal surgical team; 7/10 (70%) as unplanned emergency procedures; 6/10 (60%) in patients with established disease (>6 months). An additional 15 surgical procedures involving gut resection or ileostomy formation were performed on paediatric patients with Crohn's disease (CD) or inflammatory bowel disease unclassified (IBDU) over the same period.

Conclusions: Our robust, validated all-ages population based data highlights the extremely low volume of colectomy procedures in paediatric patients, with only 2.2% of all colectomies for UC performed in children aged < 17 years. Even when colorectal procedures for paediatric CD and IBDU are included, this contributes less than 2 colectomies per year to overall rates which are in significant decline due to the increased use of biological therapies. We recommend that colectomy procedures for patients in paediatric IBD services should be performed exclusively by, or together with, specialised adult colorectal surgeons with paediatric surgical/anaesthetic support as appropriate.

Disclosure of Interest: Plevris, N: Abbvie, Takeda Lees, C: Abbvie, Oshi Health, Gilead, GSK, Pfizer, Takeda, Vifor Wilson D: Abbvie, Ferring, Roche, Predictimmune, Takeda, Falk

Patient-parents trio exome sequencing in early-onset primary sclerosing cholangitis identifies candidate genes involved in bile salt homeostasis and immunity

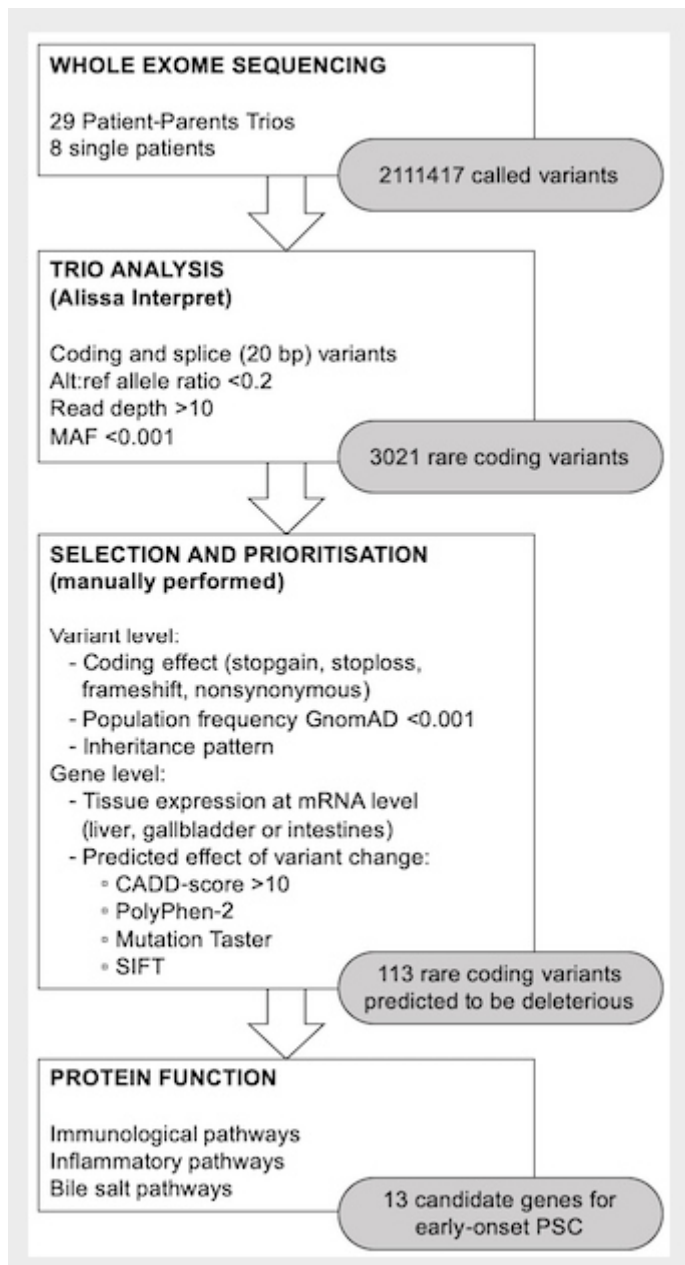
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Objectives and Study: Primary sclerosing cholangitis (PSC) is a severe liver disease leading to fibrotic destruction of the bile ducts and ultimately to the need for liver transplantation. In children the correlation with Inflammatory Bowel Disease (IBD) is close to 100%. Genome-wide association studies in adults have identified many susceptibility loci for both IBD and PSC, but a large part of the heritability remains unexplained. While several rare mutations are known to contribute to very-early-onset IBD, for PSC these variants have not been identified. We performed whole-exome sequencing (WES) in patients who were diagnosed with PSC before the age of 13 to investigate whether rare protein-altering genetic variants are associated with susceptibility to early-onset PSC.

Methods: In this multicentre study WES was performed on 95 DNA samples from 29 index patients with early-onset PSC, their biological parents and eight single early-onset PSC patients. 81% of patients had inflammatory bowel disease at the time of PSC diagnosis. We performed patient-parents trio analyses and selected rare (minor allele frequency < 0.1%) coding and splice-site variants matching recessive (homozygous and compound heterozygous variants) and dominant (*de novo*) inheritance in the children. Pathogenicity of the variants was predicted with an in-house developed algorithm (GAVIN). PSC relevant variants were selected using among others gene expression data and gene function.

Results: We identified compound heterozygous variants in genes *ABCB6*, *DACT1* and *JMJD1* in two separate trios, and in eight other trios we identified a total of 10 *de novo* variants in 10 genes with predicted pathogenic effects on protein function. Identified genes have roles in bile salt homeostasis, adaptive and innate immunity and epithelial barrier function.



[Figure. Variant selection and prioritisation]

Conclusions: We identified rare protein-altering genetic variants in 13 genes for 10 out of 29 families, that may explain a substantial part of the aetiology of PSC. The functional consequences of our newly discovered variants and the associated susceptibility to PSC will require further verification using replication studies and functional evidence.

O-010

Validation of a new score for paediatric Crohn's disease on a paediatric tertiary Hospital: The MINI-Index (Mucosal Inflammation Non-Invasive Index)

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Objectives and Study: The incidence of pediatric Crohn's disease has increased in the last years. New non-invasive tools for the prediction of endoscopic activity have been proposed to improve the selection of patients who require an ileocolonoscopy. In 2017, Turner et al, developed the MINI-INDEX (Mucosal Inflammation Non-Invasive Index) as a new clinical-analytical index in adults with high correlation with the endoscopic activity assessed by SES-CD (Simplified Endoscopic Activity Score for Crohn's Disease). Our study aims to validate the Mini-Index in the pediatric population to use it in clinical practice.

Methods: Retrospective cohort study of patients with Crohn's disease who underwent ileocolonoscopy between 2015 and 2017 in a pediatric tertiary hospital. We performed the endoscopic index SES-CD and the MINI INDEX, that evaluates in each patient the stool pattern, fecal calprotectin (mg/kg), C-reactive protein (mg/l) and erythrocyte sedimentation rate (mm/hour), obtaining a total score index between -3 and 25.

Results: A total of 96 ileocolonoscopies performed on Crohn's disease patients were included in the study. 69.8% were males and 30.2% females, with an average age \pm SD of 13.65 ± 2.78 years. Overall, the mean SES-CD score was 13.26 ± 9.25 and the median (IQR) of the Mini-Index was 16.5 (10). 15.6% had an SES-CD score < 3 (remission), 21.9% between 3-10 (mild activity) and 62.5% > 10 (moderate-severe activity). The median of the Mini-Index for each group of SES-CD was: -1 (7) in patients with SES-CD < 3 , 14 (8) in SES-CD 3-10 and 18.5 (5) in the group of SES-CD > 10 , obtaining statistically significant differences ($p < 0.001$). Furthermore, Pearson correlation was performed between the Mini-Index and SES-CD values, which was statistically significant ($p < 0.001$, $r = 0.701$). Selecting mucosal healing as a SES-CD value < 3 we performed a ROC curve for the Mini-Index obtaining an AUC of 0.985 ($p < 0.001$). The best cutoff point was a Mini-Index value < 6 ($p < 0.001$), with a sensitivity of 100%, specificity 96%, positive predictive value 83% and negative predictive value 100%. Turner et al. proposed a cut-off in the Mini-Index for mucosal healing of < 8 and we obtained the same results using < 6 .

Conclusion: Our results confirm the Mini-Index as a useful non-invasive tool in pediatric Crohn's disease to predict the inflammatory status of the mucosa with high precision. The Mini-Index could be incorporated into the clinical practice of pediatric Crohn's disease to help us to select those patients that require an ileocolonoscopy. However, further prospective studies are needed to confirm these results.

O-011

The effect of Adalimumab treatment on linear growth in children with Crohn's disease: a post-hoc analysis of the PAILOT randomized control trial

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Objectives and Study: Growth impairment is common in children with Crohn's disease. The PAILOT trial was a randomized controlled trial aimed to evaluate the effect of proactive vs. reactive therapeutic drug monitoring in children with Crohn's disease treated with adalimumab. Our aim in this post hoc analysis was to assess the effect of adalimumab treatment on linear growth in children with moderate-to-severe Crohn's disease who were followed from week 4 post adalimumab initiation until week 72.

Methods: Children 6-17 years old with moderate-to-severe Crohn's disease, naïve to biologic treatment, who responded to adalimumab induction at week 4, were assessed at week 4 and each visit during the study period (week 4, 8 and every 8 weeks thereafter till week 72) for anthropometric parameters (height, weight and body mass index, BMI Z-scores). We also analyzed the associations of these parameters with clinical disease activity, inflammatory biomarkers, fecal calprotectin and adalimumab trough concentration.

Results: Overall, 78 patients (29% females; mean age, 14.3±2.6 years) were analyzed. For the entire cohort Median weight and BMI Z-scores significantly improved from baseline (week 4) to week 72: -0.52 (IQR, -1.23-0.15) to -0.10 (IQR, -0.91-0.60) and -0.29 (IQR, -1.06-0.48) to 0.1 (IQR, -0.77-0.94), respectively; $p < 0.01$ for both. The change in height Z-score was analyzed in children with growth potential (≤ 14 years at baseline). Among 37 patients (27% females; mean age 11.9±1.9) height Z-score improved from -0.62 (IQR -1.41-0.0) to -0.3 (IQR, -1.11-0.71), $P=0.03$. A greater increase in BMI was associated with female gender ($p=0.013$), and higher PCDAI at baseline ($p=0.005$). A greater increase in weight was associated with higher PCDAI at baseline ($p=0.01$). Perianal involvement was associated with slower improvement in growth velocity ($p=0.02$). Disease activity during maintenance by means of PCDAI, CRP and fecal calprotectin was not associated with a change in anthropometric parameters.

Conclusions: Adalimumab treatment significantly improves linear growth, weight and BMI in children with moderate-to-severe Crohn's disease.

(Clinicaltrials.gov no: NCT02256462).

Development of the PICMI - the paediatric inflammatory Crohn's MRE Index: the ImageKids prospective study

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Objectives and Study: There is no validated MRE-based inflammatory index for children although Crohn's disease (CD) is more often panenteric compared to adults. The aim of the multicenter prospective ImageKids study was to develop such an index termed Pediatric Inflammatory Crohn's disease MRE Index (PICMI).

Methods: Children with newly diagnosed or established CD undergoing an MRE and ileocolonoscopy were prospectively enrolled in 22 sites globally. Extensive clinical data, SESCD, global assessments, laboratory results, and wPCDAI were recorded as well as bio-sampling including fecal calprotectin (FC). MREs were scored independently by the site radiologist and two central radiologists; the bowel was divided into 20cm segments and sections (jejunum, ileum, TI and colon). Measured variables included length of involved segments, a radiologist global assessment of inflammation on a 0-100mm visual analog score (VAS) and 9 items selected by a Delphi group of 30 international radiologists and a systematic review of the literature: wall thickness, T2 intensity, enhancement, diffusion weighted imaging (DWI), narrowed lumen, comb sign, constructed to select the most significant variables against SESCD and global assessment. The beta scores of the models were used to weight the PICMI final items.

Results: 240 children with CD were recruited, of whom 158 were used herein as the derivation cohort (age 14±2.4 years, 54% males, median disease duration (2.1 (IQR 0.3-4.3) years). Multivariable regression model retained the following items: wall thickness, DWI, ulcers, edema and comb sign, with different weights in the small bowel and colon. Five contending weighting schemes were constructed by the steering committee (table) and all five were explored on the data, first while ignoring the length of inflammation within each segment and then repeating the evaluation with the exact length (yielding 10 contending versions). All four large bowel weighting versions were highly correlated with wPCDAI ($r=0.5-0.52$; $p<0.001$), SESCD ($r=0.4-0.41$; $p=0.005$), ESR ($r=0.31-0.34$; $p=0.005$), FC ($r=0.36-0.48$; $p=0.03$) and in one of the versions also CRP ($r=0.295$; $p=0.046$). The six small bowel weighting schemes of the PICMI correlated with wPCDAI ($r=0.34-0.39$; $p<0.001$), terminal ileum SESCD ($r=0.44-0.48$, $p<0.001$), CRP ($r=0.38-0.39$; $p<0.001$) and ESR ($r=0.21-0.23$; $p<0.039$); the corresponding correlation with FC was fair ($r=0.11-0.17$, $p=0.32$). Of the different versions, the one that included the exact inflammatory length and prioritized the ileum performed best.

Conclusion: The PICMI index is being developed as a MRE tool for paediatric CD to supplement endoscopic assessment. The variables to be included in the PICMI have been selected and are in correlation with constructs of disease activity. The top three weighting schemes will be now applied to the validation cohort for selecting the final PICMI version.

	Small Bowel (Jejunum, ileum & terminal ileum)			Large Bowel (Cecum, ascending colon, transverse colon, sigmoid)	
	Version A	Version B	Version C	Version D	Version E
Wall thickness	3	1	3	3	1
DWI	9	10	9	9	6
Ulcers	6	6	6	6	9
Edema (T2)	7	4	6	6	4
Comb Sign	7	14	9	9	5

[Table contending weights of the PICMI variables]

Disclosure of Interest: The ImageKids study was supported by a grant from AbbVie.

O-013

Quantified terminal ileal motility during MR enterography as a biomarker of Crohn's Disease endoscopic activity in a paediatric population: A retrospective study

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Objectives and Study: Recent studies in adults with Crohn's Disease have shown an inverse correlation between small bowel motility and gastrointestinal inflammatory activity, as assessed by endoscopy and histology. In this retrospective study, we aimed at exploring whether a relationship between terminal ileal (TI) motility and an endoscopic endpoint is characteristically present also in CD children

Methods: A review of Great Ormond Street Hospital paediatric imaging database was performed to identify subjects with good quality MRE studies and an endoscopic assessment within 3 months from MRE studies, in order to determine the endoscopic score for disease activity (SES-CD score). Thirty eight subjects (median age 11, range 5-18) with dynamic 'cine' imaging through the terminal ileum were identified. The dynamic images were processed, blind to any clinical data, with a previously validated motility assessment algorithm (GIQuant®, Motilent, London, UK). A consultant radiologist delineated the TI on each subject within 5 cm of the ileocecal valve and the motility score derived. TI motility score was correlated against the SES-CD and the population split into 'active' and in-active groups based on SES-CD < 2 = remission.

Results: There was a significant correlation ($R = -0.45$, $P < 0.01$) between the median TI motility (0.2, range 0.05-0.6) and the median SES-CD (9.5, range 0-32). There was also a significant statistical difference between TI motility in active (0.17, range 0.05 - 0.47) and inactive (0.37, range 0.2 - 0.6, $P = 0.006$) CD children

Conclusion: Our study showed a significant inverse correlation between TI motility index and endoscopic score in children with Crohn's disease, conforming with the recent observations in adults. Moreover, the difference found between active and inactive disease suggests its potential use as a novel biomarker for disease activity. However, further prospective study in a higher number of patients is needed to confirm our findings.

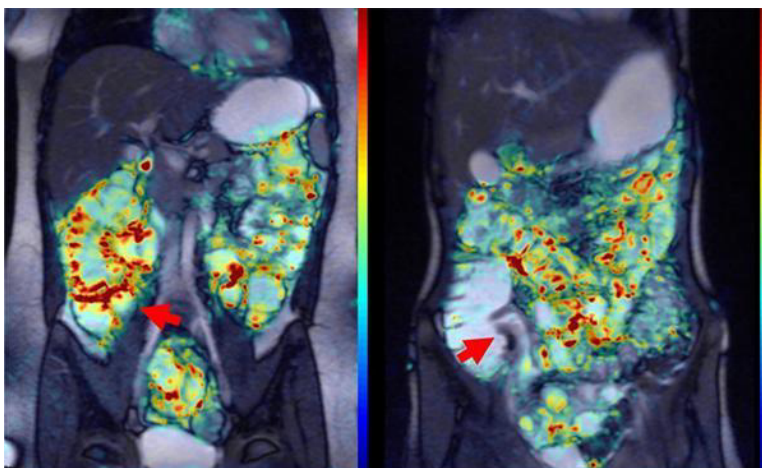


Figure: Motility map (red = high motility, blue = low) overlaid with an anatomical imaging showing the terminal ileum. The terminal ileum (left, red arrow) of a subject with a low symptom score demonstrating good motility. The terminal ileum of a patient with a high symptom score (right, red arrow).

[Motility Map]

Disclosure of Interest: A.M. is the Founder and CEO of Motilent Ltd., a medical imaging analysis company

STEP-CD study: uSTekinumab use in paediatric Crohn's disease. A multicentre retrospective study from paediatric IBD Porto group of ESPGHAN

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Objectives and Study: Ustekinumab is a fully human monoclonal antibody that blocks the p40 subunit of interleukin 12/23. Ustekinumab is effective for induction and maintenance of remission in adult Crohn's disease (CD) but data in paediatric CD is scarce. This study aims to describe the effectiveness and safety of ustekinumab in refractory paediatric CD patients in a European multi-centre cohort in real-life practice.

Methods: Retrospective review of children with CD (2-18 years old) who were treated with ustekinumab (at least one dose) from centres worldwide affiliated with the Paediatric IBD Interest and Porto group of ESPGHAN. Primary outcome was corticosteroid (CS)-free remission (defined by wPCDAI (weighted Paediatric Crohn's Disease Activity Index) < 12.5) at 6 weeks. Secondary outcomes were CS-free remission and safety at 12 weeks.

Results: a total of 104 patients (26 centres, 10 countries) were included (54 males (52%), mean age at ustekinumab initiation 15.5 years (IQR 12.7-17.4), mean previous disease duration 4.3 years (IQR 2.5-6.8)). Sixty percent of the patients had ileocolonic involvement (L3) and 24.5% perianal disease. The median wPCDAI at ustekinumab initiation was 42.5 (IQR 27.5-60). Ninety-seven percent were previously treated with anti-TNF (67% with two of them) and 22% had received vedolizumab. The most used induction strategy was an intravenous dose of 6 mg/kg (IQR 5-6) and in 93.4% of the

patients maintenance strategy was based in 90 mg doses sc every eight weeks. At week 6 (n=64) 38% of these patients were in CS-free remission. At 12 weeks (n=51) 35% of these patients maintained in CS-free remission. No deaths nor malignancies were reported during the follow-up. Three severe adverse events (clinical deterioration due to disease worsening requiring admission) and 5 minor adverse events (2 infections, 1 infusion reaction, 1 abnormal laboratory result and 1 clinical deterioration) were reported.

Conclusions: This is the largest cohort of ustekinumab use in paediatric CD patients thus far. Despite its retrospective nature and the lack of standardized treatment, we demonstrate that ustekinumab was effective and safe in a sub-cohort of anti-TNF refractory paediatric CD patients at short term follow-up. Larger cohorts as well as prospective studies are needed to confirm these results in the long term follow-up.

Top-down infliximab superior to step-up in children with moderate-to-severe Crohn's disease - a multicenter randomized controlled trial

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Objectives and Study: In newly diagnosed paediatric Crohn's Disease (PCD) patients current guidelines instruct to start exclusive enteral nutrition (EEN) or oral prednisolone in combination with immunomodulators to achieve remission. Infliximab (IFX) is proven to be highly effective in paediatric CD patients, but only used once patients are refractory, the so called step-up (SU) treatment strategy. However, evidence is emerging IFX is more effective the sooner it is initiated. We hypothesize that initiation of IFX directly, i.e. top-down (TD) after diagnosis of moderate-to-severe CD, results in higher long term remission rate. Our aim is to compare efficacy of TD and SU treatment in newly diagnosed moderate-to-severe paediatric CD

Methods: For this international randomized controlled trial (RCT) 100 patients aged 3-17 years, with new-onset, untreated CD with weighted paediatric CD activity index (wPCDAI) >40 were included in 12 centres. All patients were randomly assigned to TD or SU treatment. TD treatment consisted of 5 IFX (CT-P13) infusions of 5 mg/kg (0, 2, 6, 14, 22 weeks) combined with azathioprine (AZA). After 5 infusions, IFX was stopped while continuing AZA. SU treatment consisted of induction therapy with EEN or oral prednisolone (at physician and patient/parents discretion) combined with AZA as maintenance treatment. In both groups, IFX could be (re)started on predefined conditions. Primary endpoint of this study was sustained clinical remission (wPCDAI < 12.5) at week 52 without need for additional therapy or surgery. Secondary endpoints included patient rate using IFX at week 52, as well as clinical remission, endoscopic detection of mucosal healing (SES-CD < 3) and low fecal calprotectin (Fcal) levels (< 250 ug/g) at week 10.

Results: Three out of 100 patients didn't start with the study after randomization (n=97; TD:50 vs SU:47). There were no significant differences within the two groups at baseline. Median age was 15.0 years [IQR 11.7-16.6] in TD, and 14.2 years [IQR 12.0-16.3] in the SU group. Median wPCDAI was 55 [IQR 45-65] and 57.5 [IQR 47.5-67.5] in the TD vs SU group, respectively. For preliminary analysis of the primary endpoint data of 75/97 patients were available. At week 52, TD treatment resulted in sustained clinical remission for 18/37 [49%] of the patients compared to 5/38 [13%] of SU patients (p=0.001). After induction therapy IFX was (re)started in 13/37 [35%] TD patients compared to 27/38 [70%] SU patients within 52 weeks (p=0.001). At week 10, TD resulted in significant more patients in clinical remission (TD: 24/41 [59%] vs SU: 15/42 [36%], p=0.037) as well as endoscopic remission (47/97 consented to repeated endoscopy; TD: 17/28 [61%]; vs SU: 5/29 [17%]; p=0.001). Lastly, significantly more TD patients had a low Fcal level (n=44; TD: 9/23 [39%] vs SU: 4/21 [19%], p=0.005).

Conclusion: We are the first to compare TD IFX to SU treatment in an RCT of paediatric CD patients. Although this analysis is preliminary, TD treatment was superior to SU in achieving sustained clinical remission (wPCDAI < 12.5) without the need for additional therapy or surgery at week 52. Moreover, at week 10 significantly more TD patients were in clinical and endoscopic remission and had low Fcal levels compared to SU patients.

Poster presentations

P-001 (Poster of Distinction)

GM-CSF producing NCR⁻ ILC3s directly activate neutrophils in the intestinal mucosa of inflammatory bowel disease

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Objectives and Study: Inflammatory bowel disease (IBD) is characterized by dysregulated mucosal immune responses associated with genetic, environmental and microbial factors. Innate lymphoid cells (ILCs) are emerging immune cells which mediate immunity against pathogens and maintain tissue homeostasis. The purpose of this study was to investigate the distribution of ILC subsets and myeloid cells in the colonic mucosa of IBD patients and define the interactions between ILCs-myeloid cells using a murine model of the dextran sulfate sodium-induced colitis.

Methods: A cohort of 111 children with the diagnosis of IBD (Crohn disease: n=82, ulcerative colitis: n=29), along with non-inflammatory 40 control children, was recruited. We analyzed the distribution of ILCs and myeloid cells in 179 colonoscopic biopsies from non-IBD and IBD patients by flow cytometry. We also validated the interaction of ILCs and myeloid cells using dextran sulfate sodium-induced colitis model.

Results: We observed increase of natural cytotoxicity receptors (NCR)- ILC3s and neutrophils, but a decrease in NCR⁺ ILC3s in IBD patients (p=0.0495). Neutrophils and NCR⁻ ILC3s in colonic IBD mucosa had a significant positive correlation (r=0.4005, p=0.0058). In the mice with induced colitis, neutrophils and NCR⁻ ILC3s were increased and had positive correlation. Intracellular cytokine staining revealed that NCR⁻ ILC3s in the colons from colitis induced mice expressed a higher level of granulocyte-macrophage colony-stimulating factor (GM-CSF). Blockade of GM-CSF improved disease symptoms by inhibiting activation of neutrophils.

Conclusion: We have demonstrated that GM-CSF producing NCR⁻ ILC3s directly activate neutrophils in the intestinal mucosa of IBD. Further studies are needed to elucidate the ILCs functions in the pathogenesis of inflammatory bowel disease.

P-002 (Poster of Distinction)

Shifts in bacterial community function are associated with Short Chain Fatty Acid (SCFA) pathways during nutritional therapy in paediatric Crohn's disease patients

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Objectives and Study: Changes in gut bacterial community structure are associated with Crohn's Disease (CD) and response to therapy. A recently completed randomized controlled trial (RCT) showed improved sustained remission with the Crohn's Disease Exclusion Diet + Partial Enteral Nutrition (CDED+PEN) as compared with Exclusive Enteral Nutrition (EEN).¹

Methods: We examined changes in the microbiome functional network in patients reaching remission with nutritional therapy. Stool samples from 53 CD patients reaching remission after 6 weeks of dietary treatment were collected at weeks 0, 6 and 12 and whole shotgun sequence data were obtained. In total, 146 CD patient samples were combined with 26 healthy controls (previously published by Lewis et al.²), and characterized using HUMAnN2. Reactions, substrates and products for genes with an enzymatic commission were input into an unsupervised Bayesian analysis of community metabolism (BiomeNet). Statistical analysis of community metabolism were performed using R. Non-negative matrix factorization (NMF) and Structural topic models (STM) were used to identify patient-associated microbial metatypes.

Results: Unsupervised analyses revealed two metatypes. All healthy controls possessed one metatype (M1). CD patients possessed a mixture of two metatypes (M1 & M2), with mixtures related to time in treatment, with 48% belonging to M1 at baseline before dietary therapy. At week 6, the number of M1 samples had increased to 63% and further increased to 74% M1 at week 12 which was closer to healthy controls. Among the pathways identified within metatypes, one differed substantially between the two metatypes; the key reactions involve the metabolism of various sugars.

Using NMF and STM, we identified five communities; two were predominant in M1, and the other three were predominant in M2. The communities identified in M1 samples had high levels of Bacteroidetes, including *Odoribacter*, *Alistipes*, *Prevotella*, *Barnesiella* and *Bacteroides* as well as increases in Firmicute taxa *Eubacterium*, *Ruminococcus*, *Oscillibacter*, *Clostridium*, *Faecalibacterium* and *Roseburia*. The Proteobacteria were decreased in M1. M2 samples were characterized by Enterobacteriaceae.

Genes involved in butyrate formation were also associated with M1 and M2. Genes involved in the 4-aminobutyrate pathway, and crotonoyl-CoA to butyrate pathway, ($p=0.03$ to 0.0001) were associated with M1. M2 was associated with genes involved in the acetyl-CoA pathway as well as *ato* genes ($p<0.001$), involved in the degradation of SCFA.

Conclusion: Diet-induced remission samples were more similar to healthy controls, having shifted away from the baseline. The functional network, associated with active disease, changes as patients progress to remission at week 6 and sustain the remission through week 12. The butyrate-related change in community function is attributable to distinct shifts in bacterial species abundance. Genes significant for the M1 butyrate pathway appeared to be driven by *Bacteroides* and *Clostridium*, while genes significant for M2 butyrate pathways were driven by taxa in Enterobacteriaceae notably *Citrobacter*, *Escherichia* and *Enterobacter*.

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P-003

Distinct metabolite profiles of patients with paediatric Crohn disease

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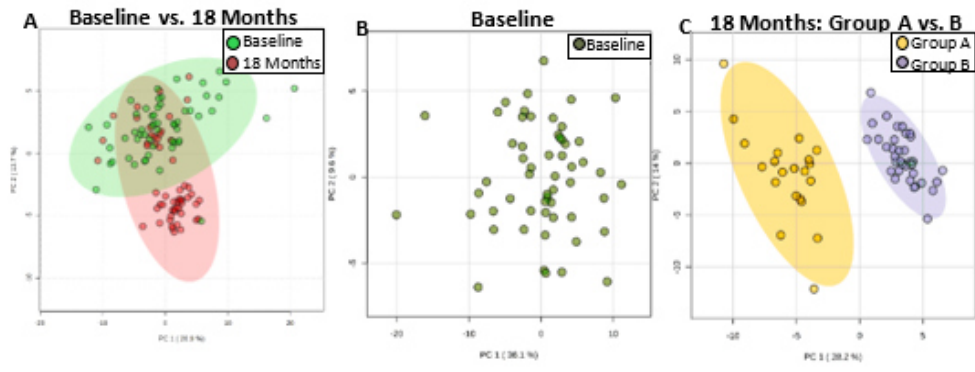
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Objectives and Study: The uses of metabolomics remain relatively under-explored in paediatric Crohn disease (pCD). Metabolite changes may precede clinically detectable changes in disease state or may help define subgroups of patients and explain pathogenesis. Appropriate characterization of disease can enable earlier more accurate intervention, potentially helping to prevent disease flares.

Methods: A multicentre, prospective cohort observational study (ImageKids), conducted to develop magnetic resonance enterography (MRE) indices for pCD, also assessed changes in serum metabolites over time. Fifty-six newly diagnosed and previously known patients (33 males) were recruited; MRE, clinical data, and serum were collected at baseline and after 18 months. Serum specimens were analysed with liquid chromatography followed by mass-spectroscopy. Resulting metabolite profiles were analysed using supervised and unsupervised multivariate methods and correlated with clinical course, treatments, and MRE findings. Quantitative enrichment analysis, referencing the small molecule pathway database, identified metabolic pathways significantly altered over time. The Image Kids study was supported by a grant from AbbVie.

Results: Principal component analysis showed a shift in serum metabolite clusters for some patients between time points (Fig 1A). While no clear separation was seen at time zero (Fig 1B), two distinct clusters were evident at the 18 month time point, named groups A and B (Fig 1C). Partial least square discriminate analysis identified key serum metabolites driving the separation (with 5 principal components retained $Q^2=0.98$, $R^2 = 0.998$, Accuracy = 1.0). Unpaired students' t-tests identified 79 metabolites (out of 128 found in patient serum) significantly different between groups ($p < 0.05$ after adjustment for false discovery rate). Group B showed increased concentrations of metabolites positively associated with DNA methylation capacity, as well as increased immunomodulatory polyamines. Physician global assessment, body mass index Z-score, and weighted pCD activity index (wPCDAI) scores did not correlate with metabolite clusters, and groups were a mix of both newly diagnosed and previously known CD patients. Patients in group A were more likely to have both inflammation and damage identified on MRE at 18 months ($p=0.016$). After adjusting for sex and history of bowel resection, group A patients had higher C-reactive protein at baseline ($p=0.007$) and were more likely to have received antibiotics at baseline ($p=0.004$). Patients in metabolite group B were somewhat less likely to have a history of bowel resection at study completion ($p=0.124$). Quantitative enrichment analysis of metabolic pathways shifted between baseline and 18 months revealed two unique subgroups of patients with differences in 52 metabolic pathways ($p < 0.05$).

Conclusions: Serum metabolomics was able to define two distinct groups at the 18-month time point and can be used to identify subpopulations of paediatric CD patients. These metabolites correlate with defined patient characteristics, including need for treatment, inflammatory markers, and possibly need for surgery. Key metabolites may assist in defining patient subgroups and have potential use as biomarkers of disease.



[Figure 1. Principal Component Analyses of Serum Metabolites]

Disclosure of Interest: ImageKids was funded by Abbvie.

P-004 (Poster of Distinction)

Altered intestinal microbiota is present in newly diagnosed IBD patients and significantly differs from that of healthy siblings and healthy controls

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Objectives and Study: The etiology of inflammatory bowel disease (IBD) is unclear, but clinical and experimental data suggests that gut microbiota plays an important role in the pathogenesis. First-degree relatives of patients with IBD are at increased risk of developing IBD themselves. Studying siblings of patients with IBD may provide insights into genetic and non-genetic factors relevant to IBD pathogenesis, since it minimizes the influence of genetic background and family diet. Indeed, it has been observed recently in adult patients that CD patients share some aspects of the intestinal dysbiosis with their relatives. Therefore, the aim of this study was to determine intestinal microbiota in newly diagnosed IBD patients and compare it to patients' healthy siblings and healthy unrelated controls.

Methods: Newly diagnosed paediatric IBD patients (n=19, 68.4% CD, mean age 14.8 ± 0.65 years) and their unaffected healthy siblings (n=20, mean age 12.8 ± 0.85 years) were recruited at the Referral Centre for Paediatric Gastroenterology and Nutrition at the Children's Hospital Zagreb. Unrelated healthy controls (n=19, mean age 10.7 ± 0.8 years) were recruited by circular e-mail sent to staff who accepted their children's participation. All participants older than 9 years of age and/or their parents gave written consent. Stool samples of all participants were collected. Terminal restriction fragment length polymorphism (TRFLP) analysis was performed on fecal samples from all participants. DNA was extracted from stool samples, 16S rRNA genes were amplified by PCR and the PCR products were digested with HhaI and MspI restriction enzymes. Length of T-RF was determined using ABI 310 genetic analyzer (ThermoFisher Scientific, USA.) The bacterial diversity was assessed by the Shannon diversity index (SDI).

Results: There was no difference in duration of breastfeeding (p=0.606), time of weaning (p=0.994), number of siblings (p=0.055), mode of delivery (p=0.881) and owning of pets (p=0.973) between the three groups. Based on TRFLP results of HhaI/MspI-digested 16S rDNA, microbial diversity of the gut microbiota in IBD patients was reduced compared to that of healthy siblings and healthy controls (Table 1). Post-hoc analysis revealed that the difference was significant only for IBD-patients vs. healthy siblings. No significant difference in microbial diversity was found between healthy siblings and healthy controls. In IBD patients, altered intestinal microbiota (dysbiosis) was present, with reduced presence of genus *Eubacterium*, *Lactobacillus*, *Enterobacter*, *Clostridium* cluster XIVa and *Clostridium* cluster IV, while increased presence of genus *Streptococcus*, *Prevotella* and *Escherichia*, compared to healthy siblings and healthy controls were present.

Conclusions: Newly diagnosed paediatric patients with IBD show significantly less diverse microbiota and microbial composition compared to healthy siblings and healthy controls. To our knowledge, this was the first study that compared intestinal microbiota of newly diagnosed paediatric IBD-patients with healthy siblings and healthy controls.

Shannon index	IBD (n=19)	Healthy siblings (n=20)	Healthy controls (n=19)	p-value
Mspl digestion, mean (SD)	2.11 (0.12)	2.45 (0.85)	2.44 (0.74)	0.018
Hhal digestion, mean (SD)	1.75 (0.12)	2.14 (0.81)	1.99 (0.66)	0.013

[Table 1. Comparison of gut microbial diversity of study participants]

Disclosure of Interest: Iva Hojsak received payment/honorarium for lectures or consultation from BioGaia, Nutricia, Nestle, GM pharma, Chr Hansen. Sanja Kolaček received fees for lectures from Abbott, AbbVie, Fresenius, Mead and Johnson, Nestle, Nutricia, Oktal Pharma. Other authors have no conflict of interest to declare. This study was part of a research project IP-2014-09-3788 funded by Croatian Science Foundation.

Fecal calprotectin is inferior to mucosal calprotectin mRNA expression in its association with disease severity and effectiveness of week 4 corticosteroid-induced remission in treatment naïve pediatric ulcerative colitis

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Objectives and Study: The calprotectin heterodimer S100A8/A9 amplifies mucosal inflammatory responses in Ulcerative Colitis (UC). Patients with higher colonic S100A8/9 expression experience lower rates of mucosal healing with infliximab. We aimed to test for correlation between fecal and mucosal calprotectin levels and disease severity at baseline, and define biologic processes and treatment responses associated with elevated calprotectin levels in treatment naïve pediatric UC.

Methods: The global pattern of gene expression was determined using RNA Sequencing in rectal biopsies from 206 treatment naïve UC patients and 20 healthy controls enrolled at diagnosis at 24 sites, and fecal calprotectin was measured by ELISA. Gene set enrichment analysis identified biologic processes associated with high calprotectin production. The Pediatric UC Activity Index defined clinical severity, and the Mayo endoscopic sub-score mucosal severity. Mild patients received mesalamine and moderate-to-severe patients received corticosteroids per protocol and week 4 clinical remission was determined.

Results: Rectal S100A8 expression was strongly associated with rectal S100A9 expression ($r=0.978$, $p<0.001$), but only weakly associated with fecal calprotectin ($r=0.235$, $p=0.005$). Rectal S100A8 mRNA expression was associated with both clinical ($r=0.551$, $p<0.001$) and mucosal ($r=0.517$, $p<0.001$) severity, while fecal calprotectin protein exhibited a modest association with clinical ($r=0.198$, $p=0.02$) but not mucosal ($p=0.146$, $p=0.08$) severity. We observed a wide range of calprotectin expression within clinical severity sub-groups. Median (IQR) rectal S100A8 expression increased from 27(14,41) transcript per million (TPM) in patients with mild activity to 90(37,202) in those with moderate-to-severe activity, $p<0.0001$, while fecal calprotectin increased from 1629(994,4026) mcg/gm to 2404(1235,3836) mcg/gm ($p=0.03$). We therefore asked whether treatment responses differed between high and low calprotectin expressers. Week 4 remission rates with mesalamine did not vary with baseline calprotectin. However, week 4 remission rates with corticosteroids decreased with higher expression of rectal S100A8, from 76% in the lowest two quartiles to 45% in the highest two quartiles ($p=0.0002$). In contrast, baseline fecal calprotectin protein levels failed to correlate with corticosteroid response. Genes differentially expressed between UC patients within the highest versus lowest quartile for rectal S100A8 expression at ≥ 1.5 fold-change with a false discovery rate of 0.001 defined pathogenic processes. These included heightened anti-microbial, TNF ($p=9.252E-52$), and granulocyte responses ($p=2.012E-94$), and dysregulation of colorectal adenoma genes ($p=2.07E-42$), in high S100A8 expressers.

Conclusion: Higher rectal S100A8/A9 expression at UC diagnosis is associated with greater induction of antimicrobial and TNF signaling and reduced corticosteroid responses. Patients with amplified calprotectin dependent mucosal inflammatory responses may benefit from alternative approaches directly targeting this pathway.

P-006 (Poster of Distinction)

Increased faecal short chain fatty acid content with Infliximab therapy in paediatric crohn disease

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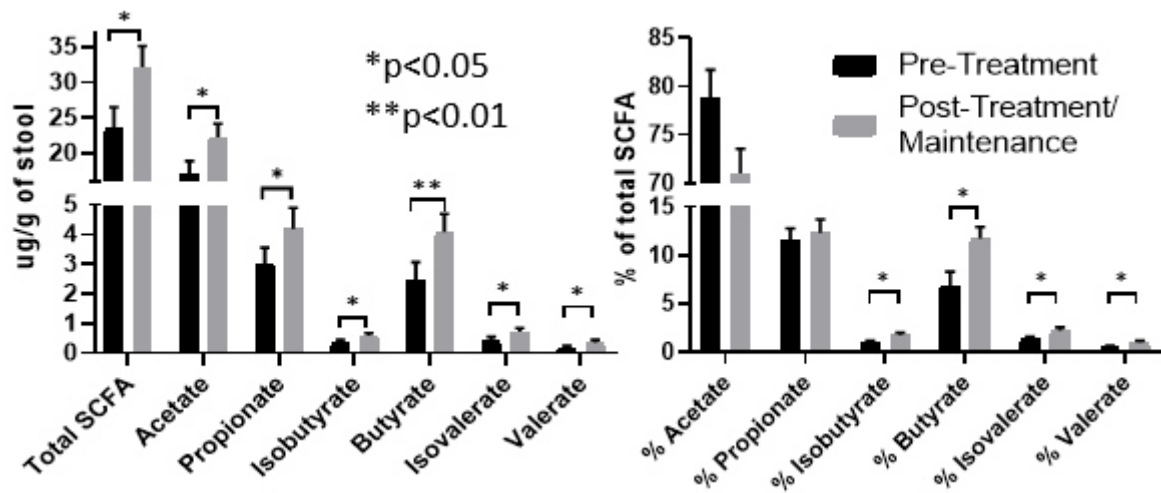
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Objectives and Study: Faecal short chain fatty acids (SCFA) are primarily produced through microbial fermentation, have multiple beneficial effects (including on gut immune homeostasis), and serve as a preferred fuel source for colonocytes. SCFA concentrations have been shown to be altered in inflammatory bowel diseases (IBD), and administration of select SCFA has shown some therapeutic effect. Variations in SCFA stool content in paediatric IBD have been minimally researched, particularly in response to therapy.

Methods: A multi-centre prospective Infliximab dose to level pharmacokinetic study during induction therapy in paediatric Crohn disease patients (IDeaL) was conducted. Thirty-five patients (18 males) were recruited from three Canadian paediatric tertiary-care IBD centres and received five Infliximab doses over 22 weeks. Stool was collected and analysed at study initiation and completion for SCFA and faecal calprotectin (FCP; as a surrogate marker for intestinal inflammation). SCFA were extracted from stool and content analysed using gas chromatography; FCP content was analysed using ELISA. Breusch-Pagan tests for homoscedasticity identified variables requiring transformation, and simple linear regression was used to test for correlations of SCFA content with FCP, disease activity, and treatment outcomes.

Results: Faecal samples were available just prior to doses one and five for 26 participants (74%, 11 males). Total faecal SCFA content significantly increased after four doses of Infliximab, as did each of the six individually identified SCFA ($p < 0.05$ after adjustment for false-discovery rate; see Figure). The proportion of butyrate, isobutyrate, valerate, and isovalerate significantly increased in stool samples collected pre-dose one to pre-dose five ($p < 0.05$). An increase in disease activity, as assessed by physician global assessment, was negatively associated with propionate ($p=0.05$), valerate ($p=0.021$), and total stool SCFA content ($p=0.043$), with borderline negative association with isobutyrate content ($p=0.052$). The presence of stricturing or penetrating disease was marginally associated with a higher total SCFA concentration ($p=0.06$). At all time-points, a higher weighted paediatric Crohn disease activity index (wPCDAI) score was associated with decreased SCFAs, in both total and individual concentrations with the exception of propionate ($p < 0.05$). Simple endoscopic score for Crohn disease (SES-CD) was negatively associated with valerate content ($p=0.002$).

Conclusions: Infliximab therapy was associated with increased faecal SCFA content as well as an increased diversity of SCFA, as proportions of less abundant SCFA significantly increased. Differential associations with disease and symptom status suggest distinct effects among the SCFA, with valerate content showing the most consistent negative association with disease activity and endoscopic findings. These changes may reflect increased microbial diversity resulting from effective treatment and accompanying changes in inflammation state, diet, or host-microbe interactions and may serve as biomarkers or stimulate development of novel therapies, targeting SCFA-producing bacteria.



[Stool Short Chain Fatty Acid Content & Proportions Before and After 22 Weeks Infliximab Treatment]

Disclosure of Interest: IDEaL was funded by Janssen and the Women & Childrens Health Research Institute (WCHRI). Authors M.W. Carroll, W. El-Matary, A.M. Griffiths, H.Q. Huynh, & E. Wine have previously or currently serve as advisers for Janssen.

P-007

The relationship between villous length and duodenal protein expression of CYP3A4 in children with Crohn's disease

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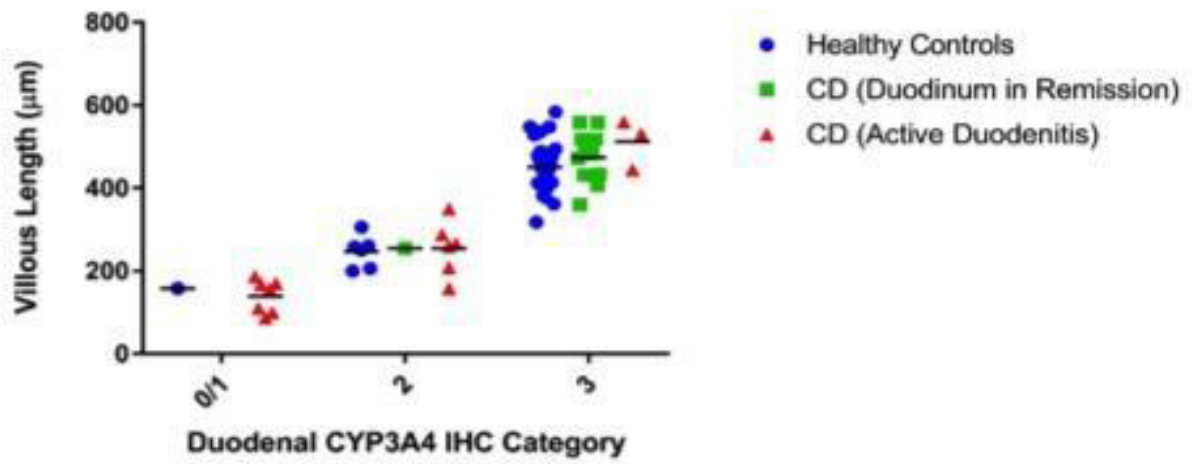
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Objectives and Study: The villous brush border of the duodenum expresses cytochrome P450 enzymes (CYPs) that are capable of metabolizing orally administered drugs, before they reach systemic circulation. Duodenal inflammation, more common in pediatric Crohn's disease (CD) than adult CD, is generally thought to downregulate CYP expression. Specifically, mRNA expression of CYP3A4, the most abundantly expressed CYP in the human small intestine, is decreased in CD. The objective of this investigation was to characterize the relationships between CYP3A4 protein expression, inflammation, and villous length in the duodena of children with and without CD.

Methods: Fresh, flash frozen duodenal mucosal biopsies from treatment-naïve children with CD and without inflammatory bowel disease (Control) were assessed for inflammation by two independent pediatric pathologists (n=99, 1-19 years). Villous length was measured using Infinity Analyze software. In a subset of samples (n=65), immunohistochemistry (IHC) staining for CYP3A4 was performed, using a polyclonal antibody from ThermoFisher Scientific. Postnatal liver tissue and normal intestinal mucosa were used as external and internal positive controls, respectively. Intensity of IHC staining along the villi was scored as grades: 1) complete/marked loss of staining; 2) patchy/moderate loss of staining; 3) normal staining, enriched at the apical brush border of villi. Using ANOVA, villous length and IHC staining were compared among Control and CD samples with (CD-active) and without (CD-remission) duodenal pathology, and Spearman's correlation was used to assess relationships between IHC grade and villous length; $\alpha < 0.05$ (JMP v12).

Results: Of the 37 children with CD, 18 had active disease in the duodenum. Villous length (μm) was significantly shorter in CD-active (289 ± 140 , n=18) than CD-remission (503 ± 69 , n=19) or Control (476 ± 60 , n=62); $p < 0.001$. Villous length did not correlate with age ($p=0.4$) and was comparable between CD-remission and Control ($p=0.3$). The pattern of CYP3A4 protein expression was weaker and patchier in CD-active (n=16) vs. CD-remission (n=14) or Control (n=35). The proportion of abnormal CYP3A4 staining (grades 1 & 2) was 81% in CD-active, 7% in CD-remission, and 20% in Control. Independent of disease status, a positive association was observed between CYP3A4 staining and villous length (Figure 1; $p < 0.05$).

Conclusion: Villous length, which appears stable after 1 year of age, may be an important covariate in the interpretation of protein expression studies in Crohn's disease. Significantly reduced CYP3A4 protein expression was noted in actively inflamed duodena in CD, compared to CD in remission or Controls. However, the observed positive association between CYP3A4 IHC staining and duodenal villous length, independent of diagnosis or inflammatory status, suggests that villous blunting, not inflammation *per se*, may be responsible for this finding. Changes in mucosal CYP3A4 protein expression, as a function of villous integrity, may be a relevant determinant of oral drug bioavailability for CYP3A4 substrates (e.g., budesonide, midazolam) in active Crohn's disease vs. disease in remission.



[Figure 1 Duodenal CYP3A4 protein expression and villous length; IHC 0/1 & 2 denote abnormal staining]

P-008

Increased frequency of regulatory T cells in pediatric inflammatory bowel disease at diagnosis: a compensative role?

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Objectives and Study: Regulatory T cells (Tregs) play a critical role in maintaining immune homeostasis. We aimed to investigate two main types of Tregs, CD4+FoxP3+ and Tr1, in pediatric subjects with inflammatory bowel disease (IBD) at diagnosis and after clinical remission.

Methods: Peripheral blood Tregs were analysed in 16 children with Crohn's disease (CD), 19 with ulcerative colitis (UC), and 14 healthy controls (HC). Two cocktails of fluoresceinated monoclonal antibodies were used to discriminate between CD4+FoxP3+ and Tr1.

Results: We observed in both CD and UC groups a higher frequency of Tr1 at diagnosis compared to controls, which decreased at follow-up compared to diagnosis, in particular in UC. Similarly, in UC patients the percentage of CD4+FoxP3+Tregs markedly decreased at follow-up compared to the same patients at diagnosis and to HC. CD4+FoxP3+Tregs expressing the markers of activation CTLA-4+ and CD62L+ were increased in both groups at clinical remission.

Conclusion: This study shows that IBD children present at diagnosis an increased frequency of circulating Tregs, probably as a compensative reaction to tissue inflammation. During the remission, the Tregs frequency diminishes and concurrently their activation status increases. However, the high Tregs density at diagnosis is not sufficient to counteract the inflammation in childhood IBD.

Disclosure of Interest: AS served as member of advisory board for the following companies: D.M.G, Valeas, Angelini, Miltè, Danone, Nestlé, Sucampo, Menarini. EM served as member of advisory board for the following companies: Abbvie, Angelini, Bioprojet, Ferring, Menarini, Milte, Valeas; GM served as member of advisory board for the following companies: Merck, Biogen, Novartis, Aegerion. CG is member of advisory board for Nemysis.

P-009 (Poster of Distinction)

IL-17-related signature genes are linked to human necrotizing enterocolitis

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Objectives and Study: Necrotizing enterocolitis (NEC) is the most frequent life-threatening gastrointestinal disease experienced by premature infants in neonatal intensive care units. The difficulty for neonatologists is to detect early clinical manifestations of NEC. One approach would be to apply early diagnostic tools that could be used to identify preterm infants most at risk of developing NEC or in a diagnostic dilemma of suspected disease, by identifying specific markers for NEC. In the last decade, the development of high-throughput sequencing of RNA transcripts (RNA-Seq) has become state-of-the-art for transcriptional profiling of differentially expressed genes. The objective of the present study was to take advantage of RNA-Seq data obtained previously from the analysis of intestinal specimens of preterm infants diagnosed with NEC (Tremblay et al., BMC Medical Genomics 9:6, 2016) to identify biological and functional processes that could lead to more insight into the pathogenesis of NEC in premature infants.

Methods: Information on intestinal samples and RNA-Seq analyses has been provided previously (Tremblay et al, 2016). Briefly, samples were obtained from premature infants having undergone bowel resection. The diagnoses were confirmed by pathologists and clinical staging of NEC were based on the criteria of Bell. Preterm patients who had undergone bowel resection for stage III acute NEC constituted positive NEC cases and preterm patients who had undergone resection for diseases other than NEC made up the control (CTRL) group. We used the Illumina HiSeq2000 to investigate the gene expression profiles of the ileum of preterm infants with NEC vs without NEC (CTRL). Data were analyzed with Ingenuity Pathway Analysis (IPA: Ingenuity Systems Inc.) and ToppCluster to identify functional pathways enriched in NEC neonates.

Results: Gene set enrichment analysis indicated that the most significant canonical pathways over-represented in NEC neonates were associated with innate immune functions, such as altered T and B cell signalling, B cell development, lymphocyte and leukocyte migration, the role of pattern recognition receptors in the recognition of bacteria and viruses, autoimmune response and IL-17 signalling. Interestingly, we also identified that the expression of major inflammatory genes regulated by IL-17 were highly modulated in NEC neonates. These IL-17 signature genes include pro-inflammatory cytokines (IL-8, IL-6 and GM-CSF), chemokines (CXCL5 and CXCL10), antimicrobials (DEF5A, DEF6A, LCN2 and mucins) and matrix metalloproteinases (MMP1 and MMP9).

Conclusion: In conclusion, our gene expression profile analysis revealed a predominantly altered innate immune response in the intestine of NEC neonates. Our observations suggest that the intestines of NEC neonates have been subjected to an uncontrolled and excessive inflammatory response. Moreover, we identified that IL-17 signalling could be a central player in the pathogenesis of NEC, as shown by the highly modulated expression of its signature genes in NEC preterms. Although IL-17 and its pro-inflammatory effectors are known to be involved in the pathogenesis of diverse autoimmune and inflammatory diseases, the precise role of IL-17 signalling in the development of NEC needs further investigation.

P-010

Exploring the effects of enteral nutrition and curcumin upon intestinal microbiota using an *in vitro* model

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Objectives: Exclusive enteral nutrition (EEN) is a well-established therapy to induce remission in children with IBD. Although many reports show intestinal microbiota changes subsequent to EEN, the significance of these changes remains unclear. The objective of this study was to evaluate the effects of enteral formula (EF) and curcumin upon the intestinal microbiota using an *in vitro* model of the gut.

Methods: A well-established *in vitro* model of the gut, featuring single-stage continuous colonic fermentation was utilized. Stool samples collected from children with Crohn disease were used as the inocula. The impact of EF was assessed using six vessels simulating the proximal colon, by first enabling all the vessels to reach a standardized steady state with optimum conditions in a complete growth medium followed by treating three models with EF + curcumin and three with EF + curcumin + fibre. The substrates were subjected to gastrointestinal digestion, similar to that in the human gut before presentation to the colon. Metabolic changes were determined using chromatographic techniques to measure short chain fatty acids (SCFAs) and polyphenolic metabolite concentrations throughout the fermentations. Microbiome structural and functional changes were assessed by whole genome sequencing followed by bioinformatics and statistical analysis.

Results: Higher concentrations of fibre in the complete medium increased the total number of bacteria and EF increased bacterial richness (alpha-diversity). The proportions of different bacterial species were influenced by the composition of the fibre (with increased beneficial *Faecalibacterium* and *Bifidobacterium*, but also other species such as *Paenibacillus*). However, comparison of the two EF did not show significant bacterial changes, indicating that the lack of fibre didn't negatively impact microbial structure *in vitro*. Chemical analysis revealed that the curcumin was used by the gut bacteria, albeit to a greater extent in the absence of fibre. In comparison to baseline, bacterial functions associated with the metabolism of vitamin C, vitamin B7, and some key amino acids and carbohydrates, were significantly altered by both test treatments. There was an increase in genes responsible for synthesis of butyrate (reflected in the SCFA profile) and vitamin B7. Fibre in general resulted in a decrease in bacterial functions associated with synthesis of potentially pro-inflammatory lipopolysaccharides. The presence of curcumin appeared to increase bacterial genes associated with degradation of xenobiotic compounds and/or increased generation of metabolites that may have a beneficial effect on gut health.

Conclusion: An established *in vitro* gut model may be suitable to assess the effects of EF interventions upon intestinal microbiota from vulnerable populations such as children with Crohn Disease. These preliminary data indicate that curcumin-fortified EF may beneficially modulate gut microbial structure and functions.

Disclosure of Interest: ASD - Advisory Board membership for AbbVie, Janssen, Sanofi

P-011

Stool preparation under anaerobic conditions contributes to retaining obligate anaerobes for faecal microbiota transplantation

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Objectives and Study: Gut microbiota dysbiosis is associated with ulcerative colitis (UC) pathogenesis. In UC patients, an increase in *Enterobacteriaceae* and *Enterococcaceae* and decrease in *Clostridium* cluster XIVa have been reported. Faecal microbiota transplantation (FMT) has variable efficacy in treating active UC in randomized clinical trials; dysbiosis correction might contribute to treatment efficacy. In general, healthy gut microbiota consists of obligate anaerobes sensitive to oxygen; thus, blending the donor's stool under aerobic conditions may diminish obligate anaerobes. However, anaerobic handling of the donor's stool may retain obligate anaerobes and enhance the clinical effect of FMT. The objective of this study was to investigate whether an anaerobically prepared stool suspension retains more viable obligate anaerobes than a conventional aerobically prepared suspension.

Methods: Faecal samples were collected from 16 healthy adult donors and transferred under an anaerobic condition using an airtight container including a deoxidizer (Anaeropack®). Samples were handled inside an anaerobic glove box in which the oxygen concentration was maintained at less than 1% by replacing air with nitrogen and were divided into two portions. Each aliquot was then diluted with normal saline and blended for 30 s either in the anaerobic glove box (anaerobic-prep) or in room air (aerobic-prep). Samples were collected at three time points: before blending (S_0), 1 h after anaerobic-prep (S_{An}), and 1 h after aerobic-prep (S_{Ae}). Then, microbiota analysis was performed using 16S and 23S rRNA-targeted reverse transcription quantitative polymerase chain reaction, enabling quantitative detection of live bacteria in stool samples. The bacterial count ratio (BCR) before and after blending was compared between the anaerobic-prep (S_{An}/S_0) and aerobic-prep (S_{Ae}/S_0) groups for each bacterial group, including dominant obligate anaerobes (*Clostridium coccooides* group, *C. leptum* subgroup, *Bacteroides fragilis* group, *Bifidobacterium*, *Atopobium* cluster, and *Prevotella*) and facultative anaerobes (*Enterobacteriaceae* and *Enterococcus*).

Results: In the *C. coccooides* group (*Clostridium* cluster XIVa), the BCR was significantly higher in the anaerobic-prep group [median, 0.51; interquartile range (IQR), 0.29-0.65] than in the aerobic-prep group (median, 0.29; IQR, 0.15-0.37; $p < 0.01$). In the *B. fragilis* group, a significantly higher BCR was observed in the anaerobic-prep group (median, 0.75; IQR, 0.50-1.91) than in the aerobic-prep group (median, 0.46; IQR, 0.38-1.18; $p < 0.01$).

For the two facultative anaerobic bacteria (*Enterobacteriaceae* and *Enterococcus*), the median BCR in each group was 1.98 (IQR, 1.06-2.97) in the anaerobic-prep and 1.21 (IQR, 0.69-3.02) in the aerobic-prep groups. There was no significant difference ($p=0.23$).

Conclusions: The superiority of our anaerobic-prep method in retaining obligate anaerobes such as the *C. coccooides* group and *B. fragilis* group was shown. These bacteria are believed to maintain intestinal homeostasis and exert anti-inflammatory effects. Thus, our anaerobic preparation might contribute to improving the outcome of FMT by effectively retaining obligate anaerobes.

P-012

Environmental risk factors predisposing to Inflammatory Bowel Disease (IBD) in Asian children - a multicentre study in Malaysia

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Objectives and Study: Rising incidence of IBD in developing countries implicates the importance of environmental influences in addition to genetic predisposition in the pathogenesis of IBD. We aimed to identify environmental risk factors predisposing to childhood IBD from a population with low prevalence of IBD.

Methods: Children with a confirmed diagnosis of IBD diagnosed at less than 18 years from three (University Malaya Medical Centre, Selayang and Penang Hospital) centers in Malaysia were matched with 2 controls by age, gender and ethnicity. Data on family history, diet, infections, vaccination, living conditions and socioeconomic status were obtained.

Results: Seventy children with a confirmed diagnosis of IBD (38 Crohn's disease [CD]; 32 ulcerative colitis [UC]) were matched with 140 controls. In multivariate model, a positive familial history of IBD (CD: $p = 0.045$, UC: $p = 0.001$); previous hospital admission for acute gastroenteritis (AGE; CD: odds ratio [OR] 6.4 [95% confidence interval 1.6 - 24.7], UC: OR 3.9 [1.005 - 15.0]); antibiotics more than 4 times in a year (CD: OR 4.3 [1.1-16.1]), UC: OR 3.4 [1.1 - 10.1]); maternal infection (CD: p -value 0.045) and tonsillectomy (CD: p -value 0.044) increased the odds of developing IBD. Using bottled water for drink and cooking (UC: OR 0.156 [0.04 - 0.59]) was the only protective factor identified.

Conclusion: A positive family history was risk factor for IBD while tonsillectomy for CD. Previous admission for AGE suggests infectious agents initiating the development of IBD. Antibiotics usage and maternal infection play a role in altering intestinal microbiota in IBD.

P-013

Circadian clock gene disruption may be a causative event in inflammatory bowel disease flares and a target for treatment

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Objectives and Study: Pathophysiological mechanisms active in inflammatory bowel disease (IBD), such as mucosal barrier repair, innate and adaptive immune responses, intestinal motility and gut microbiome, all exhibit diurnal variations. Chronic disruption of the external cues to the molecular clock, augment the inflammatory response.

We recently found that newly diagnosed, naïve to treatment, young IBD patients show reduced clock gene expression not only in inflamed and non-inflamed intestinal tissues, but also in systemic blood. This reduction in clock gene expression correlated with disease activity.

Methods: IBD patients were evaluated upon diagnosis naïve to treatment in comparison to the medically treated state. Disease activity scores and current medical treatment recorded, C-reactive protein (CRP) and fecal calprotectin (Fcal) levels were measured and peripheral blood was analyzed for clock gene (CLOCK, BMAL1, CRY1, CRY2, PER1 and PER2) expression.

Results: In the naïve treatment state, clock gene expression (CLOCK, BMAL1, CRY1, CRY2, PER1 and PER2) was reduced in WBC. Eleven IBD patients (5 with Crohn's Disease, 5 with Ulcerative Colitis and one IBD-U patient) from our preliminary cohort were followed-up while under treatment. Two with active disease and nine in clinical remission. Of those achieving clinical remission, clock gene (CLOCK, BMAL1, CRY1, CRY2, PER1 and PER2) expression levels increased in WBC.

Conclusions: Young, newly diagnosed, naïve to treatment, IBD patients show reduced clock gene expression in inflamed and non-inflamed intestinal mucosal samples and in systemic blood. Under treatment, after gaining clinical remission, they present up-regulation of clock gene expression in WBC. Altogether, these findings may suggest that clock gene reduction is an early event in IBD pathogenesis and treatment rectifies clock gene expression.

P-014 (Poster of Distinction)

Paediatric inflammatory bowel diseases and risk of serious infections: A nationwide register-based cohort study

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Objectives and Study: Childhood onset inflammatory bowel disease (IBD) is believed to be a more severe disease with more use of immunosuppression than adult-onset IBD, but there is little information on risk of serious infections (defined infections in inpatient care) in patients with paediatric IBD (PIBD, < 18 years). We performed a population-based cohort study to estimate absolute and relative risks for serious infections in patients with PIBD.

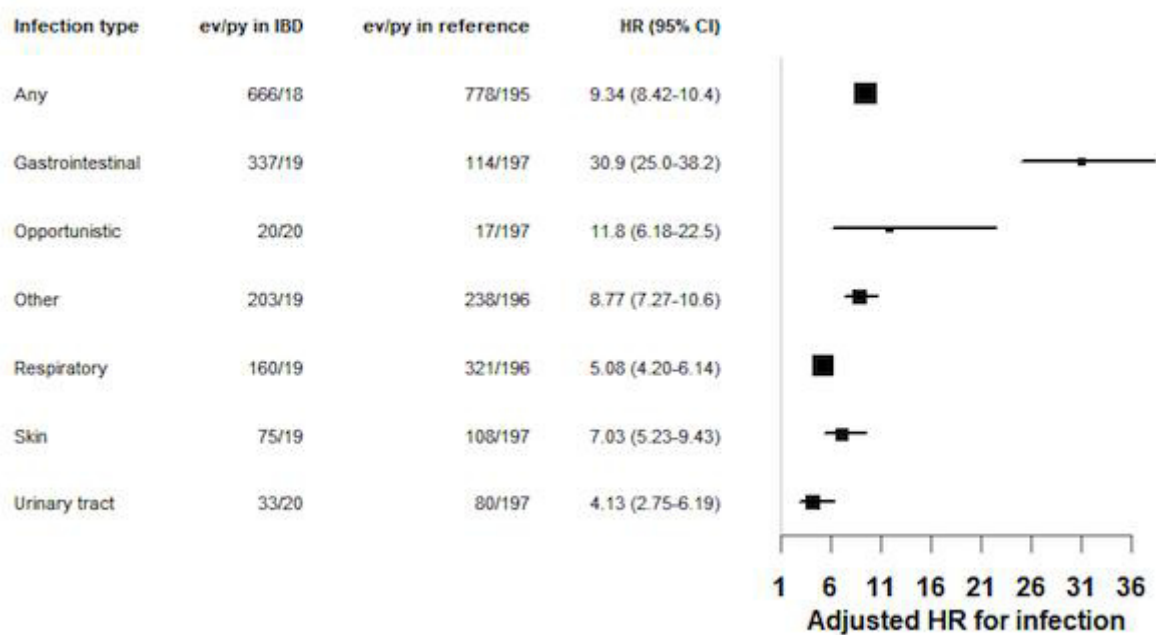
Methods: We identified children (< 18 years) with a first diagnosis of IBD in the Swedish nationwide health registers (2002-2017; n=6039) and individuals from the general population matched for sex, age, calendar year, and place of residence (reference group; n=58418). Study participants were followed until first serious infection (overall and first in a category), 31 December 2017, or their 18th birthday, whichever occurred first. Hazard ratios (HR) for serious infections were estimated using Cox regression separately in patients with ulcerative colitis (n=2422), Crohn's disease (n=2454), and IBD unclassified (n=1163).

Results: During 17,608 person-years of follow-up, 666 serious infections (37.8/1000 person-years) occurred among the patients with IBD compared with 778 serious infections in the reference group (4.0/1000 person-years; adjusted HR (95% CI), 9.34 (8.42-10.4)). HRs (95% CIs) were increased for patients with ulcerative colitis 8.28 (7.04-9.74), Crohn's disease 9.36 (7.91-11.1), and IBD unclassified 11.8 (9.42-14.8).

Compared to matched reference individuals, PIBD patients exposed to thiopurines, anti-TNF, or both all had an increased risk of serious infections. HRs (95% CIs) were 8.62 (7.43-9.99), 6.00 (4.16-8.65), and 5.48 (3.74-8.03), respectively (please note that HRs across episodes of different drug exposures are not directly comparable with each other).

Apart from a very high relative risk of gastrointestinal infections resulting in hospitalization (Figure 1), patients with PIBD were also at an increased risk of serious infections at all other locations and for opportunistic infections (11.8 (6.18-22.5, Figure 1)).

Conclusion: PIBD patients, including those exposed to modern IBD drugs including immunomodulators and anti-TNF, have an increased risk of serious infections compared to the general population. A measure of this excess risk is important for contextualizing clinical trials in the future.



[Figure 1. Risk of infections in PIBD compared to general population by site or type of infection.]

Disclosure of Interest: Dr. Olén has been PI on projects at Karolinska Institutet partly financed by investigator-initiated grants from Janssen, Ferring, Takeda, and Pfizer. None of those studies have any relation to the present study. Dr Ludvigsson coordinates a study unrelated to the present study on behalf of the Swedish IBD Quality Register (SWIBREG). That study has received funding from Janssen.

P-015

Predictors of outcome in children with Crohn's Disease

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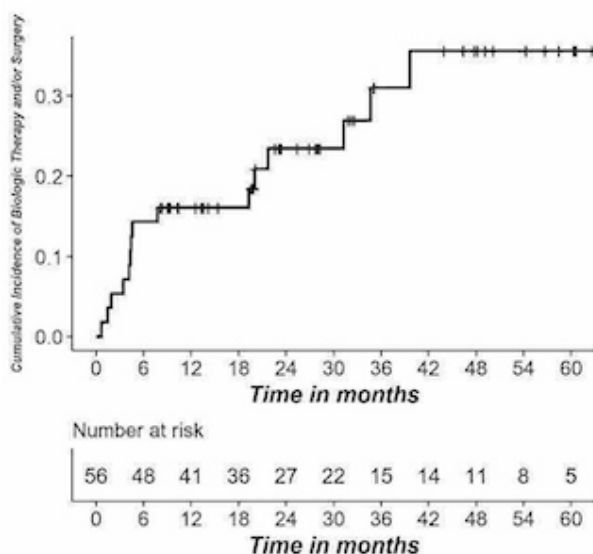
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Objectives and Study: Data regarding the incidence and the risk factors either for biologic therapy or for surgery in children with Crohn's disease (CD) are still lacking. The aims of this study were to determine the cumulative incidence of need for biologics and for surgery and to identify associated risk factors in a cohort of children with CD.

Methods: We conducted a retrospective chart review of 56 children diagnosed with CD from January 2013 through June 2017 with at least 12 months follow up. Age at onset; gender; family history; anthropometric data; clinical, laboratory, endoscopic, and histological findings at diagnosis, timing of therapeutic regimens, and small bowel US were thoroughly investigated. Data regarding disease localization according to Parisclassification and disease activity indexes were also collected. The primary outcome was defined as need for biologic therapy and for intestinal surgery. Statistical significance was predetermined as $p < 0.05$. Percentages were rounded to the nearest whole numbers.

Results: The 56 enrolled patients [M/F: 31/25; median age: 12.8 yrs (range 6.7-16.8)] were divided into two groups: Group A, represented by 41 (73%) patients who did not receive biological treatment and/or surgery; Group B, represented by the remaining 15 (27%) patients subjected to biological treatment and/or surgery. Univariate Cox models showed that family history (hazard ratio [HR] 3.02, $p=0.04$), C reactive protein (CRP) (HR 1.016, $p < 0.001$) and terminal ileal thickening (HR 1.14, $P=0.02$) were associated with increased risk for intestinal surgery and/or use of biologics. Age, gender, anthropometrics, disease activity, disease behaviour and location, and extraintestinal manifestation were not associated with the need for more intensive therapy. Kaplan-Meier survival estimates of the cumulative incidence of surgery and biological therapy were 36.6% (95% CI = 17.2% 49.9%) at 5 years from the diagnosis of MC (Figure 1).

Conclusion: In children with CD, our preliminary data suggests that family history, CRP, and terminal ileal thickening evaluated by US at diagnosis are independent risk factors for biologic therapy and bowel surgery. In addition, in contrast with previous studies, we found a low cumulative rate of bowel surgery with a similar use of biologic therapy.



[Figure 1. Kaplan-Meier estimates for risk of Biologic Therapy and/or Surgery]

P-016

Predictors for poor outcome of hospitalizations in children with inflammatory bowel disease

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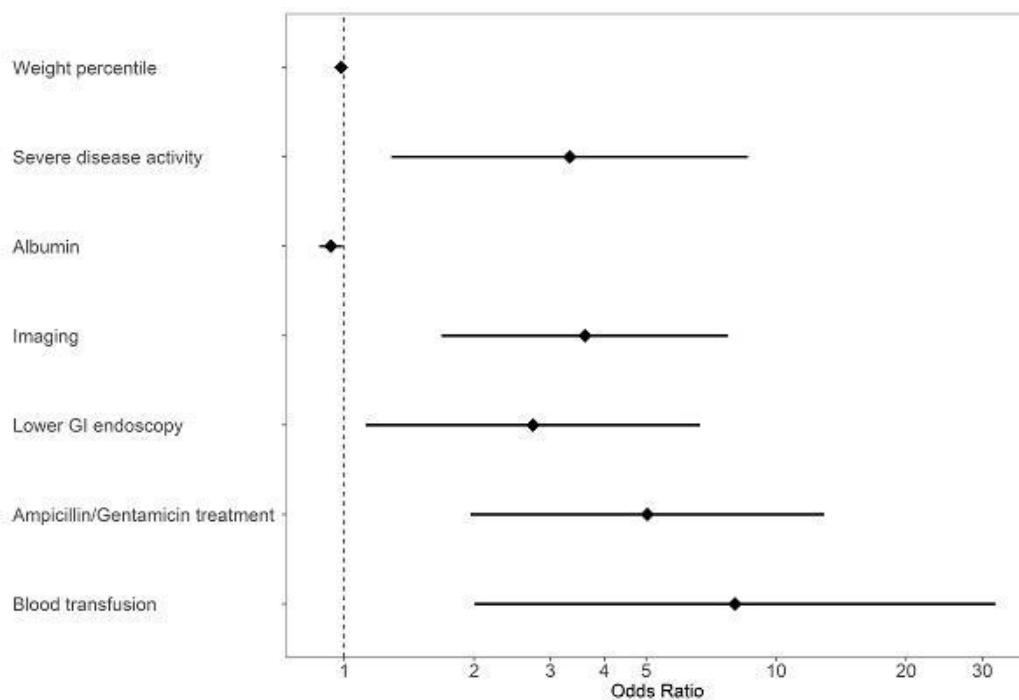
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Objectives and Study: Inflammatory bowel disease (IBD) exacerbations may lead to prolonged and complicated hospitalizations, that may affect the quality of life of the patients, as well as health costs. The aim of the study was to describe characteristics of exacerbation-related hospitalizations and to identify predictors for poor outcome of hospitalizations in children with IBD.

Methods: We performed a retrospective cohort study of all children who were hospitalized due to IBD exacerbation, during the years 2004-2017 in a tertiary medical center. Demographic and disease characteristics before and during hospitalization were documented, as well as course of hospitalization including laboratory, diagnostic work-up and management. Poor outcomes were defined as prolonged hospitalization of 7 days and longer and need for surgery during hospitalization.

Results: We included a total of 181 hospitalizations of 78 IBD children with a median (IQR) age of 14.8 (11.8-16.2) years. Among them, 53 (67.9%) were Crohn's disease patients and 25 (32.1%) were ulcerative colitis. In a multivariate analysis, severe disease activity at hospitalization (OR=3.33, P=0.013), lower weight percentile (OR=0.98, P=0.009), treatment with antibiotics (OR=5.03, P=0.001), blood transfusion (OR=8.03, P=0.003), need for endoscopy (OR=2.73, P=0.027) and imaging during hospitalization (OR=3.61, P=0.001) were predictors for prolonged hospitalization. Surgical intervention was performed in 16 cases (8.8%), with penetrating (OR=7.73, P=0.019) and stricturing disease (OR=12.38, P< 0.001) as predictors.

Conclusions: We recognized predictors for poor outcomes of hospitalizations in children with IBD. Early recognition of children at risk for poor outcome during hospitalizations may improve the management of these children.



[Predictors for prolonged hospitalizations of children with IBD]

P-017 (Poster of Distinction)

Risk factors for developing paediatric inflammatory bowel disease in an Irish prospective cohort

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Objectives and Study: A worldwide increase is observed in the incidence of paediatric inflammatory bowel disease (PIBD). Growing evidence suggests that environmental factors play a key role in the development of IBD in genetically susceptible individuals. Both protective and risk factors have been identified across numerous studies. The Determinants and Outcomes in Children and Adolescents with IBD (DOCHAS) study is the first prospective cohort study assessing potential risk factors for developing PIBD in Ireland.

Methods: Children aged 0-16 years attending Children's Health Ireland (CHI) at Crumlin presenting with symptoms of IBD were recruited to DOCHAS between January 1st 2012 and March 30th 2019. CHI at Crumlin is the single national referral centre for PIBD in Ireland, allowing the total capture of all Irish PIBD patients. A standardized case report form was completed with participants and their families at enrolment. Questions assessed environmental risk factors including birth history, exposure to smoking, urban/rural/farm dwelling, appendicectomy, use of antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs), as well as family history of autoimmune disease. Following endoscopy, patients were categorised as IBD or non-IBD (Controls). IBD patients were diagnosed and classified according to the Porto criteria and the Paris Classification of IBD. Data was exported from the study database into GraphPad Prism 8.1.0 for statistical analysis.

Results: 792 patients were recruited. 188 (24%) were controls, 320 (40%) had CD, 232 (29%) had UC, 21 (3%) had Atypical UC and 31 (4%) had IBD-unclassified (IBD-U). Mean age \pm standard deviation at diagnosis was 12 ± 3 years in CD, 12 ± 3 in UC patients. Males were more likely to be diagnosed with CD (M:F ratio: 2.6:1) than with UC (1.1:1, $p < 0.0001$). Paediatric IBD was associated with a caesarean section delivery (21 % [control] vs 31% [CD] and 28% [UC], $p=0.03$). Patients with a personal or family history of autoimmune disease (atopic disease, ankylosing spondylitis, autoimmune thyroid disease, coeliac disease, multiple sclerosis, rheumatoid arthritis, SLE/lupus, psoriasis or type 1 diabetes) were more likely to be diagnosed with CD than UC (74% vs. 58%, $p=0.0002$). This was also found in patients previously diagnosed with autoimmune disease (39% [CD] vs. 28% [UC], $p=0.008$). Patient history of atopic disease was more often associated with CD than with UC (34% vs. 21%, $p=0.0007$), as was autoimmune disease in first-degree relatives (37% vs. 25%, $p=0.002$). No significant differences were found between CD and UC regarding exposure to smoking, urban/rural/farm dwelling, appendicectomy, previous antibiotic or NSAID exposure and a reported history of previous infectious gastrointestinal disease.

Conclusions: In the Irish population, caesarean section delivery and a personal or family history of autoimmune diseases were significantly associated with PIBD, especially with CD. Ongoing prospective research is needed to further elucidate these phenotype-specific associations.

P-018

Increasing incidence of pediatric inflammatory bowel disease based on the prospective nation-wide Hungarian Pediatric IBD Registry (HUPIR)

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Objectives and Study: The incidence of inflammatory bowel disease (IBD) is increasing worldwide, but only a few countries have prospective nation-wide incident cohort registry to evaluate the incidence of pediatric IBD. Our aim was to evaluate the incidence of pediatric IBD in Hungary and analyze the incidence in different age groups.

Methods: Newly diagnosed pediatric IBD patients (ages 0-18 years) are recorded in HUPIR and are followed-up yearly. The data are collected from all the 27 gastroenterological centres where IBD patients are diagnosed and treated in Hungary. The questionnaire at diagnosis includes epidemiological data, initial symptoms, diagnostic work-up, disease extension, disease activity (PCDAI, PUCAI), and initial therapy. All cases are validated by an IBD expert (G.V.), and children are excluded if there is missing information on ileocolonoscopy, or if in case of normal ileocolonoscopy, upper endoscopy and radiology. We analyzed the incidence rate between 1st January 2007 and 31st December 2016. The age- and sex-specific demographic data for calculating incidence were obtained from the Hungarian Central Statistical Office. Descriptive statistical methods were applied for data analysis. We analyzed the incidence in three age-groups (younger than 10, between 10-14 and older than 15 years). The statistical analysis was performed in Excel, Microsoft.

Results: Between 1st January 2007 and 31st December 2016, 1541 new IBD cases were identified, 958 (62.12%) Crohn's disease (CD), 491 (31.86%) ulcerative colitis (UC) and 92 (5.97%) IBD-unclassified (IBD-U) patients. From the 958 CD patients, there were 942 patients with known gender, 544 male and 398 female patients (1:1.37) which shows the male domination in CD. In UC and IBD-U the gender distribution was equal. Incidence of IBD increased from 7.1/10⁵ to 11.6 /10⁵ during the 10 years, which was 63.38 % increasing. We detected the increasing incidence in every type of IBD. In CD, the incidence increased from 4.3/10⁵ to 6.8/10⁵, in UC from 2.3/10⁵ to 4.0/10⁵, and in the IBD-U from 0.5/10⁵ to 0.8/10⁵. The median age at diagnosis was 13.6 (range between 0.9 and 18.0) in CD, 12.7 years (range between 1.2 and 18.0) in UC and 12.5 (range between 1.58 and 17.66) in IBD-U. The median age was equal in male and female (13.3 vs 13.3). The incidence in children under 10 years did not change during the 10 years, but the incidence in children over 10 years has increased. In CD, the incidence increased more intensively in children above 15 years (9.1/10⁵ to 19.2/10⁵) than in children aged between 10-14 years (6.3/10⁵ to 10.8/10⁵). In UC, there was no difference in the velocity of increase between the two age groups (3.43/10⁵ to 6.43/10⁵ vs. 4.28/10⁵ to 7.89/10⁵).

Conclusion: The incidence of pediatric IBD increased in Hungary by 63.38% (6.3%/year) between 2007 and 2016. The incidence of IBD did not change in children younger than 10 years old, which could be explained by the dominating genetic background as a cause of the disease. The increase in the incidence of pediatric IBD was due to the increase in the age-group above 10 years, reflecting an increasing role of the environmental factors in the development of the disease.

P-019

Diagnostic work-up of paediatric IBD in a nation-wide Hungarian paediatric inflammatory bowel disease registry (HUPIR)

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Objectives and Study: In about 5-15% of paediatric inflammatory bowel disease (PIBD) cases Crohn's disease (CD) or ulcerative colitis (UC) can not be differentiated; as a result these children are initially diagnosed as inflammatory bowel disease unclassified (IBD-U). Most of the previous epidemiological studies reported no significant change in the incidence of IBD-U. The Porto Criteria recommend upper endoscopy, ileocolonoscopy and small bowel imaging for all the children with the suspicion of IBD. Our aim was to evaluate the diagnostic work-up of PIBD and to evaluate whether the change of diagnostic work-up affected the rate of IBD-U.

Methods: Newly diagnosed paediatric patients with IBD (ages 0-18 years) are registered in this prospective, nation-wide registry (Hungarian Registry of Paediatric Inflammatory Bowel Disease, HUPIR). The questionnaire at registration includes epidemiological data, disease extension, diagnostic work-up and initial therapy. Patients registered between 1st of January 2007 and 31st of December 2016 were involved to analyse the change of diagnostic practice in Hungary, and we investigated whether the change of diagnostic practice influenced the rate of IBD-U. We used descriptive statistical methods and Chi square test for the analysis.

Results: Between 2007 and 2016 1541 children were registered, among them 92 patients were diagnosed as IBD-U (6%), 958 patients as CD (62%), and 491 children as UC (32%). The Porto Criteria were fulfilled in 37% of the CD cases, 28% of the IBD-U cases and 47% of the UC cases. Upper endoscopy was performed in 83% of children with CD, and its frequency increased significantly from 2007 to 2016 (from 61% to 95%, $p < 0.05$). The rate of ileocolonoscopy also elevated from 54% to 87% ($p < 0.05$) during the ten years. Fiftyfour percent of the patients had adequate small bowel imaging (range 42% to 68%), mostly MRE (73%). In UC, upper endoscopy was performed in 66% of patients, and its frequency increased significantly from 41% to 83% ($p < 0.05$) during the ten years. The rate of ileocolonoscopy also elevated from 45% to 75% ($p < 0.05$). Fifteen percent of the patients had adequate small bowel imaging. Upper endoscopy was performed in 77% of patients with IBD-U, and its frequency increased significantly during the ten years (from 22% to 93%, $p < 0.05$). Frequency of ileocolonoscopy also elevated from 44% to 86% ($p < 0.05$). The rate of adequate small bowel imaging was between 29% and 75%. The incidence of IBD-U increased from 0.5/100000 to 0.8/100000. Six percent of all IBD patients had IBD-U, this rate did not change significantly during the ten years (range 3 to 10%). The rate of IBD-U was 7.2% in the group with incomplete diagnostic work-up, while in the group with complete diagnostic work-up 4.2% of children had IBD-U. The difference was significant ($p < 0.05$).

Conclusions: The diagnostic practice has improved in the last ten years in Hungary, however, still less than half of the IBD cases fulfil the Porto Criteria. Mostly the small bowel imaging was lacking that is probably due to the low availability of MRE in Hungary. The improvement of the diagnostic practice was not associated with the decrease of IBD-U, however, the complete work-up may decrease the rate of IBD-U.

P-020 (Poster of Distinction)

Diagnostic accuracy of serum proteinase 3 antineutrophil cytoplasmic antibodies for paediatric patients with ulcerative colitis: a prospective multicenter study in Japan

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Objectives and Study: Various serologic markers such as perinuclear antineutrophil cytoplasmic antibodies (p-ANCA), the putative antigen is thought to be myeloperoxidase (MPO), have been reported to screen for patients with ulcerative colitis (UC). However, MPO-ANCA was found to have limited accuracy in Asian population. The antigen recognized by cytoplasmic pattern ANCA (c-ANCA) is a 29-kD serine protease from myeloid azurophilic granules that is known as proteinase 3 (PR3). Takedatsu et al reported that serum PR3-ANCA is more useful for diagnosis of UC in Japanese adult population than MPO-ANCA (sensitivity of 39.2% and specificity of 96.6%; J Gastroenterol Hepatol 2018). The aim of this study was to clarify whether PR3-ANCA is a useful serologic marker for diagnosis of UC in Japanese paediatric population.

Methods: Subjects were prospectively enrolled children under 17-year-old who visited at 12 paediatric centers in Japan between November, 2016 and February, 2018 and were divided into 4 groups such as patients with UC, Crohn's disease (CD), intestinal disease control (IDC) including IBD unclassified, Behçet's disease, and XIAP deficiency, irritable bowel syndrome and infectious colitis, and healthy control (HC). Serum PR3-ANCA was analyzed using chemiluminescence enzyme immunoassay kits (STACIA® MEBLux™ test, Medical and Biological Laboratories, Aichi, Japan). The cutoff value of the assay, as provided by the manufacturer, was ≥ 3.5 U/mL.

Results: Three hundred and sixty-seven serum samples from 148 patients with UC (median age, 12 years), 120 CD (13y), 56 IDC (10.5y), and 43 HC (10y) were examined. PR3-ANCA levels (median) in UC, CD, IDC, and HC were 1.6 U/mL, 0.2 (compared with UC, $P < 0.001$), 0.15 ($P < 0.001$), and 0.1 ($P < 0.001$), respectively. ROC analysis demonstrated an area under the curve of 0.80. The manufacturer's cutoff value (3.5 U/mL) had a sensitivity of 36.5% and specificity of 93.2% for diagnosing UC. A cutoff value of 0.8 U/mL according to the ROC curve demonstrated higher sensitivity (64.9%) and good specificity (85.3%).

Conclusions: PR3-ANCA was a useful serologic marker for diagnosis of UC in Japanese children.

Disclosure of Interest: This study was supported by Medical & Biological Laboratories Co., Ltd. Shunsuke Kurei is an employee of Medical & Biological Laboratories Co., Ltd.

P-021

Discrimination of de novo paediatric IBD from controls based on urinary and faecal volatile organic compounds analysis: Which bodily excrement is best to sniff?

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Objectives and Study: To date, the diagnosis of inflammatory bowel disease (IBD) is established by a combination of histological and endoscopic abnormalities. Endoscopy is an invasive procedure, which carries a high burden on patients, especially in children. Therefore, a novel non-invasive biomarker is needed. Analysis of volatile organic compounds (VOC) by an electronic nose device has demonstrated great potential to serve as diagnostic biomarker for paediatric IBD. It is currently unknown whether analysis of urinary or faecal VOCs provide the optimal accuracy to discriminate between IBD and controls. Therefore, in the current study we aimed to assess which bodily excrement is best to analyse, i.e. urinary or faecal VOCs, by means of Gas Chromatography-ion mobility spectrometry (GC-IMS).

Methods: For this case-control study, performed in two tertiary hospitals in Amsterdam, children aged 4-17 years and suspected for IBD, were eligible to participate. All included subjects collected a faecal and urine sample prior to bowel cleansing for the diagnostic endoscopy. The control group consisted of children suspected for IBD but without mucosal abnormalities seen during colonoscopy. Urinary and faecal VOCs of children with proven IBD were compared with those from controls by means of GC-IMS (G.A.S. Flavourspec). The data were split into two sets, 70% for training and validation and 30% as test set. Wilcoxon rank-sum test was used to find the 100 most discriminatory features. Supervised statistical models were applied to assess diagnostic accuracy of both urinary and faecal VOCs.

Results: In total, 20 children were included (10 IBD (5 CD and 5 UC, 10 age-matched controls), of which 40% were male in both groups and the median age was 14,2 years [interquartile range (IQR) 9.6-16.6] in the control group and 15 years [IQR 10.4-17.1] in the IBD group. It was demonstrated that IBD could be discriminated from controls based on faecal VOCs with an area under the curve (AUC) of 0.73 [95%CI 0.34-0.86], p-value 0.04. Comparable results were found for the discrimination of IBD from controls based on urine VOCs (AUC of 0.78 [95%CI 0.57-1], p-value 0.03).

Conclusion: We demonstrated that VOC analysis has potential to serve as a non-invasive (additional) biomarker to discriminate de novo IBD children from an intention-to-diagnose population. Analyses of urinary and faecal VOCs provide comparable diagnostic accuracies. Our findings suggest that both urinary and faecal VOC analyses may be used as potential non-invasive diagnostic biomarkers for paediatric IBD. Collection of urine may possibly be more convenient for patients rather than collection of stool samples. However, these study results need to be validated.

P-022

Performance of unrestricted faecal calprotectin in paediatric inflammatory bowel disease

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Introduction: Recommendations on the utility of faecal calprotectin (FC) are based on its use in secondary care as a non-invasive tool that can rule out Inflammatory bowel disease (IBD) in children with gastrointestinal symptoms.

The diagnostic accuracy of faecal calprotectin for PIBD in primary care has been inadequately evaluated in UK practice although has been evaluated in other healthcare systems.

Aims and Objectives: The aim of the study was to evaluate the utility of FC within a well-defined geographical area. A secondary aim of the study was to study the performance of faecal calprotectin in children with GI symptoms and evaluate the predictive value of this test within a single laboratory serving both primary care and secondary care.

Subjects and Methods: Two cohorts of children were studied over one year: children seen in primary care and children referred for GI symptoms to specialist care. FC that was measured as part of the initial work up was recorded and compared with the reference standard for IBD: endoscopic assessment or one year follow up, whichever was later.

Results: Over a one year period 1004 FC test were requested on 744 patients under the age of 18. Only those patients undergoing FC for the first time in their diagnostic pathway were included. Patients with an already known diagnosis of IBD, those with incomplete results of FC and those on whom records at 1 year were not available were excluded. 497 patients were therefore studied (53%M, 47%F). The median age of children was 13 years.

257 patients had their initial FC test requested in primary care (primary care group). 23 out of 257 patients had an endoscopic assessment. 7 patients had a final diagnosis of IBD (2% yield); 16/23 had a negative endoscopic assessment. Although 33 patients in primary group had FC >250ug/G, only 12 of these on secondary screening proceeded to endoscopic evaluation of which only 7 patients had confirmation of IBD.

240 patients had the initial FC test requested following evaluation by a specialist (secondary care group). 71 out of 240 patients in this group proceeded to endoscopic assessment. 23 had a final diagnosis of IBD (9.5% yield); 48/71 did not have features of IBD on endoscopic or histological assessment. 64 out of 240 patients had FC >250 ug/G, of which 36 were evaluated further by endoscopy and 22 had IBD. Using a FC threshold value of greater than 250ug/G, the positive predictive value (PPV) in primary care is 21% (95%CI: 15.7 - 27.9%). Using the same cut off, the PPV in specialist care is 35.3% (95% C.I 28% - 41%).

Summary & Conclusion: A positive FC result in children undergoing this test in primary care is less likely to be indicative of IBD than a positive test in children undergoing this test by a specialist. However a negative test is likely to be a true negative. The yield for a diagnosis of PIBD through faecal calprotectin in primary care is 2% compared to 9.5% in specialist clinics. These findings should influence care pathways that include the FC test to determine endoscopic assessment in children suspected with IBD.

P-023

Impaired plasmacytosis as a characteristic histological finding of very early-onset inflammatory bowel disease

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Objectives and Study: Very early-onset inflammatory bowel disease (VEO-IBD), defined as IBD diagnosed by 6-year-old, is known as a heterogeneous group of disorders that includes various Mendelian forms of IBD. There have been a few studies which elucidated the histological features of VEO-IBD, and differentiating ulcerative colitis and Crohn's disease from other cause of VEO-IBD by endoscopic and histological findings would lead to the early diagnosis and proper management in this high-risk population. This study aims to reveal the characteristic histological findings that enable the differentiation of various VEO-IBD.

Methods: Children with VEO-IBD followed at a tertiary children's hospital in Japan and their legal guardians were asked to participate in this study to retrospectively review their endoscopically biopsied mucosal histology of gastrointestinal tract. 2 board-certified pathologists and 2 certified pediatric gastroenterologists reviewed all available histological and endoscopic findings of their gastrointestinal tract. VEO-IBD patients were grouped into 3 groups by their phenotypic features; ulcerative colitis type (UCT), non-UCT with perianal disease (NUC-PD), and non-UCT without perianal disease (NUC-NPD). Their histological findings were scored by validated simple biopsy criteria (Tanaka M, et al. Scand J Gastroenterol 2000;35:281), and other features such as granuloma, apoptosis, pigment vacuolated macrophages were also documented.

Results: 35 children with VEO-IBD were evaluated in this study. Their mean age was 2.2-year-old with male to female ratio of 20 to 15. There were 11 UCT, 12 NUC-PD, and 12 NUC-NPD patients. Ulcerative colitis and Crohn's disease were strongly suggestive in 2 and 3, respectively, by validated simple biopsy criteria. Mendelian forms of IBD were diagnosed based on genetic and other supportive testings in 8; chronic granulomatous disease (5 NUC-PD), X-linked lymphoproliferative syndrome-type 2 (2 NUC-PD), autoimmune enterocolitis (1 NUC-NPD). Histology of chronic granulomatous disease associated colitis was characteristic with pigmented vacuolated macrophages, granuloma, and lack of basal plasmacytosis. X-linked lymphoproliferative syndrome type 2 had Paneth cell metaplasia and granuloma, but crypt architectural distortion and plasmacytosis were relatively mild or missing. Among all 35 subjects, apoptosis was noted in 10 (29%), and impaired plasmacytosis compared to that of ulcerative colitis and Crohn's disease was noted in 29 (83%). 11 (31%) had granuloma, and 9 of them were NUC-PD

Conclusions: Most children with VEO-IBD had atypical histology for ulcerative colitis or Crohn's disease. Impaired plasmacytosis appeared characteristic of VEO-IBD.

P-024

Double balloon enteroscopy in paediatric Crohn's disease for decision therapy and 10 years follow up

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Objectives and Study: Evaluate the feasibility, validity and safety of Double Balloon Enteroscopy (DBE) in patients of a tertiary paediatric center with CD. In addition we analysed its impact on treatment strategies, establish other diagnoses (malignancy, stenosis) in 10 years follow up. Crohn's disease (CD) is a chronic recurrent inflammatory disease that may affect any segment of gastrointestinal tract. In 60-70% of CD may involve the small bowel (SB) and present a diagnostic challenge to decision regarding therapy. DBE is one of endoscopic modality for children that allow the diagnostic and therapeutic procedures of SB disease

Methods: Between 2007-10, 20 patients (age 2-20 years) with CD diagnosis, refractory to treatment were selected to undergo SB evaluation by DBE, oral route. We used general anesthesia (children < 12 y) or deep sedation with propofol (patients >13 y). Previously all had performed radiological imaging to exclude structuring

Results: Among 20 patients 90% of had SB CD in jejunum or ileum, and 10% had solely lesion in SB, which was not detected by colonoscopy. The DBE findings were: Active duodenojejunal ulcers, ulcer healing and/or pseudo polyps, sub-stenosis and mucosal granularity. Mean length of SB examined was 220 cm beyond the ligament of Treitz (range 120 to 360cm). No significant complications were related to the procedure. Currently 14 patients are in following up, 5 children in paediatric GI clinic and the other 9 at adult GI clinic. In 10 years follow up one patient had an extra intestinal malignancy diagnosis; one had IL-10 and/or IL-10R gene mutation and one change the diagnosis to ulcerative colitis. Curiously, the proportional number of patients in therapy, particularly biologic, had decreased (tab)

Conclusions: DBE is a useful tool to make differential diagnosis in SB paediatric pathologies, especially in CD who require escalating and de-escalating treatment. DBE has a good safety profile with a low index of complications when performed in reference centers.

Patients	CD at diagnosis	10 years follow up
(n)	20	14
Sex (%)	M 65/ F 35	M 64/ F 36
	Initial therapy (%)	Current therapy at 10 years follow up (%)
5-ASA	25	7
Corticosteroid	60	28
Thiopurine/Methotrexate	80	5
IFX/ADA	70	28
No treatment	0	21
IFX: Infliximab, ADA: Adalimumab		

[Tab.Demographic data and current therapy]

P-025 (Poster of Distinction)

The newly simplified MaRIA score (MaRIAs) is as accurate as the original MaRIA in paediatric Crohn's Disease: a study from the ImageKids cohort

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Objectives and Study: The MaRIA score is the most widely used index in adults to score the degree of inflammation in Crohn's disease (CD) using magnetic resonance enterography (MRE). Recently, a simplified MaRIA (MaRIAs) was developed and validated in adults but was never evaluated in children. We aimed to compare the performance of the MaRIAs with the original MaRIA on a large cohort of children enrolled in the ImageKids study.

Methods: The ImageKids study is a prospective multicentre international study, with 22 recruiting sites worldwide. MRE and ileocolonoscopy (scored by the SESCD) were performed at baselines while recording explicit clinical, demographic and laboratory measures in electronic case-report forms (using REDCap). Each MRE was read by two central radiologists including, for instance, pre and post enhancement, T2 scoring of the edema, ulceration, wall thickness and fat stranding. Stool was measured centrally for calprotectin and serum for CRP and ESR.

Results: A total of 239 children with newly diagnosed and established CD (133 (56%) males, mean age 14.2 ±2.5 years) were included. Nineteen patients were excluded due to missing pertinent MRE data. The MaRIA and MaRIAs were calculated for 1146 involved terminal ileum and colonic segments, with comparable accuracy to reflect constructs of mucosal inflammation including SESCD, CRP, ESR, faecal calprotectin and wPCDAI (Table). The MaRIA and the MaRIAs were similarly correlated at per-patient and per-segment level (Table). The agreement between both scores was moderate (intraclass correlation coefficient ICC =0.5, 95% CI 0.34-0.61). The number of children in remission was 60 (25%) according to MaRIA, 46 (19%) according to MaRIAs (Kappa = 0.14; p< 0.001) and 47 (20%) according to SESCD.

Conclusion: The MaRIA and MaRIAs performed similarly in children from the ImageKids cohort but the agreement between the indices was limited. It is noteworthy that the MaRIA and MaRIAs require enema administration which is less feasible in children and not performed in the ImageKids cohort. The original MaRIA and MaRIAs may be used in children until the development of the pediatric MRE index (i.e. PICMI) is completed and compared with the adult indices.

	MaRIA	MaRIAs
Total SESCD	r=0.514 (P<0.001)	r=0.495 (P<0.001)
CRP	r=0.379 (P<0.001)	r=0.328 (P<0.001)
ESR	r=0.291 (P<0.001)	r=0.260 (P<0.001)
Faecal calprotectin	r=0.466 (P<0.001)	r=0.447 (P<0.001)
wPCDAI	r=0.297 (P<0.001)	r=0.262 (P<0.001)
SESCD subscore in the TI	r=0.532 (P<0.001)	r=0.538 (P<0.001)
SESCD subscore in the RC	r=0.529 (P<0.001)	r=0.537 (P<0.001)
SESCD subscore in the TC	r=0.284 (P<0.001)	r=0.340 (P<0.001)
SESCD subscore in the LC	r=0.599 (P<0.001)	r=0.575 (P<0.001)

[Table]

Disclosure of Interest: The ImageKids study was supported by a grant from AbbVie.

P-026

Very early onset inflammatory bowel disease in Asian children

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Objectives and Study: Paediatric Inflammatory bowel disease (PIBD) is a rapidly emerging disease in Asia. Very early onset-IBD (VEO-IBD), defined as onset < 6 years, has varying clinical characteristics, response to therapy and outcome compared to non-VEO-IBD. The present study aimed to determine the clinical characteristics of VEO-IBD in Asian children.

Methods: Data were extracted from Asian PIBD Research Registry which was set up in 2017. The network comprises of 11 paediatric gastroenterology centres in 7 Asian countries (Hong Kong, Malaysia, Philippines, Singapore, Sri Lanka, Taiwan and Thailand). Each PIBD centre entered clinical data into REDCAPS platform hosted by the Singapore Clinical Research Institute, anonymously. Current data was contributed by members from 5 countries. Individual Institutional review board approval was obtained.

Results: Sixty-eight (30%) of 227 children with PIBD were VEO-IBD. Males (57%) were more common than females. There were 37 (54%) ulcerative colitis (UC), 25 (37%) Crohn's disease (CD) and 6 (9%) IBD-Unspecified (IBD-U). Only 2 (3%) children has first degree relative with IBD. IBD genotype was done in 5 (8%) children. Comparing to non-VEO-IBD patients, VEO-IBD are more likely to present with bloody diarrhoea (73% vs. 42%, $p < 0.001$). Other common symptoms are chronic diarrhoea (57%), weight loss (46%), and abdominal pain (32%). Extraintestinal manifestations were infrequent; with arthritis / arthralgia being the commonest (8%) in VEO-IBD group. C-reactive protein was lower in VEO-IBD (Median 12 vs. 26, $p=0.038$), compared to non-VEO-IBD. Hypoalbuminaemia and anaemia does not differ between age group. According to Paris classification, children with VEO-UC have significantly more extensive (79% vs. 67% pancolitis, $p=0.015$) and severe disease (37% vs. 14% PUCAI score >65 , $p=0.024$) as compared to non-VEO-UC. Children with VEO-CD, had significantly more colonic involvement (71% vs. 33%, $p=0.027$) compared to non-VEO-CD. No difference in upper gastrointestinal tract and perianal disease was observed between both groups.

Conclusions: Asian children with VEO-IBD consisted a higher proportion among PIBD patients as compared to Caucasian. UC and colonic CD is the predominant phenotype among VEO-IBD, with bloody diarrhoea as the predominant symptoms.

P-027

Clinical features of very early-onset inflammatory bowel disease in Japan, a single centre pilot study

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Objectives and Study: It has been reported that clinical features of very early onset inflammatory bowel disease (VEO-IBD) present differently from those associated with older-onset IBD. Additionally, since the genetic background differs between Japanese and Western populations, this may result in altered clinical features. The aim of this study was therefore to evaluate the clinical features of VEO-IBD in Japan.

Methods: We retrospectively reviewed disease type, medical history, and genetic test results from the medical records of patients with VEO-IBD who visited the paediatric department at Gunma University, Japan between April 2013 and March 2018.

Results: Ten patients were analysed (5 male : 5 female), and the age of IBD onset was between 0 months and 6 years (median : 2 years 3 months). These included 2 neonatal onset cases (less than 1 month post-partum) and 3 infantile onset cases (less than 2 years old). Endoscopic findings showed typical ulcerative colitis (UC) in 3 cases and intestinal Behçet's disease in 1 case. The other 6 cases were diagnosed as unclassified IBD. There was a family history of the disease in 3 cases. As for disease location, the oral cavity was affected in 3 cases (aphthous stomatitis, gingivitis, oral candidiasis), the terminal ileum in 2 cases, and the colon in all 10 cases. Anal involvement was noted in 3 cases. No cases showed granuloma pathologically, whereas apoptosis was observed in 2 cases. As for extraintestinal lesions, exanthema was noted in 4 cases and moyamoya disease was identified in 1 case. Growth disorders were recorded in 4 out of 10 patients at the first visit. Genetic testing was performed in 6 out of the 10 cases and genetic abnormalities (*SAMD9* · *IL10RA* · *IKBA*) were found in 3 of these cases, none of which had a positive family history of IBD. In the group with genetic abnormalities, the age at onset was younger (mutation: 1 to 9 mo.; no mutation: 3 to 4 yo.), the frequency of anal lesions was higher (2 cases with mutation, 0 cases without mutations), and the frequency of growth disorders was also higher (3 cases with mutation, 1 case without mutations) than in the group without genetic mutations. All patients with genetic mutations died of infections.

Conclusions: A high incidence of colonic lesions was seen in the VEO-IBD cases studied herein, as shown in previous reports on Western populations. The frequency of monogenic IBD was high in cases with skin lesions. The prognosis of the monogenic cases was poor. Family history was less frequent in cases of monogenic IBD, and this low prevalence of family history might represent differences in the genetic background of Japanese versus Western populations.

P-028

HLA-B51 in inflammatory bowel disease; Are there clinical implications?

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Objectives and Study: Human leukocyte antigen (HLA)-B51 allele has been thought to be the most important genetic factor of Behçet's disease(BD). When the Behçet's disease(BD) involves the alimentary tract, symptoms and signs mimic Crohn's disease and sometimes it is very difficult to differentiate two conditions. In this study we investigated the prevalence of HLA-B51 in inflammatory bowel disease and tried to analyse the clinical significance of HLA-B51 in inflammatory bowel disease.

Methods: Among patients diagnosed with Crohn's disease or Ulcerative colitis at Severance Children's Hospital from March 2012 to December 2018, 100 patients who tested HLA-B51 were finally enrolled. Clinical data, laboratory findings were collected. The HLA-B51 positive ratios were investigated according to the diagnosis and clinical characteristics were compared between HLA-B51 positive and negative groups.

Results: Seventy Crohn's disease and 30 Ulcerative colitis patients were enrolled. HLA-B51 was positive in 22 (31.4%) of Crohn's disease patients and 2 (6.7%) of Ulcerative colitis patients ($p = 0.007$). Fourteen (35.9%) female IBD patients and 10 (16.4%) male IBD patients showed positive HLA-B51($p = 0.026$). More than half of female Crohn's disease patients (52.2%) were HLA-B51 positive. The age of disease diagnosis was not different between HLA-B51 positive and negative groups. Family history of inflammatory disease, extra-intestinal manifestations and cumulative risk of surgery or biologics use were not different between two groups. In Crohn's disease, HLA-B51 was not associated with disease location or growth failure. However, negative HLA-B51 was associated with stricturing or penetrating disease behavior than inflammatory behavior. ($p = 0.0017$)

Conclusion: Female Crohn's disease and mild disease behavior might be associated with HLA-B51.

P-029

Nutritional status and food intake in paediatric IBD patients at diagnosis significantly differs from healthy controls

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Objectives and Study: The aim of this study was to assess anthropometric measures, body composition and dietary intake in children and adolescents with newly diagnosed inflammatory bowel disease (IBD) and compare them to the age, sex and area of residence matched healthy controls. This was a prospective cross-sectional study.

Methods: Newly diagnosed IBD patients (n=89) and healthy controls (n=159) who were ≤18 years were included. Anthropometric measures, body composition and food intake in the last month were assessed.

Results: Mean energy intake differed significantly between ulcerative colitis (UC) patients and healthy controls (7780.9±2774.5 kJ vs. 10198.3±4409.5 kJ; p=0.003), but not between Crohn's disease (CD) patients and healthy controls (8915.4±3377.6 kJ vs. 10198.3±4409.5 kJ; p=0.202). Significantly lower intake of all macronutrients and dietary fiber was found between UC patients vs. healthy controls. In CD patients, significant difference was found only for animal proteins and fruits. Lower intake of calcium was detected in both CD and UC patients. There was no significant difference in body fat percentage between CD and UC patients vs. healthy controls (19.3±7.6% in CD; 18.5±7.6% in UC; 20.7±7.7% in controls; p=0.239). However, both CD and UC patients had significantly lower lean mass-for-age z-scores compared to healthy controls (0.2±1.4 SD in CD; 0.4±1.2 SD in UC; 1.2±1.4 SD in controls; p< 0.001*).

Conclusion: This study showed significantly lower intake of energy, macronutrients and various micronutrients in patients with UC compared to healthy controls, while patients with CD had lower intake of fruits, calcium and animal protein. Furthermore, altered anthropometry, and more importantly, body composition in both CD and UC patients, has been shown at the time of diagnosis. This study contributes to the still scarce literature on diet and anthropometry in paediatric patients with IBD and indicates that specific nutritional interventions should be implemented early after diagnosis.

	CD (n=49)	UC (n=40)	Healthy controls (n=159)
Age, mean (SD)	14.6 (2.6)	14 (3.7)	14.7 (2.3)
Male, n (%)	29 (59.2)	23 (57.5)	80 (50.3)
BW, mean (SD)	51.5 (14.6)	51 (16.8)	59 (14.2)
BH, mean (SD)	163.2 (14.7)	161.1 (18.7)	167.4 (11.9)
BMI, mean (SD)	19.6 (2.8)	18.2 (2.8)	20.7 (3.2)
Duration of symptoms in months, mean (SD)	7.6 (2.1)	4.2 (1.0)	-

[Table 1. Baseline characteristics of enrolled patients]

BM- body weight; BH- body height; BMI- body mass index; SD- standard deviation

Keywords: inflammatory bowel disease, children, adolescents, diet, anthropometry

Disclosure of Interest: Iva Hojsak received honorarium for lectures or consultation from BioGaia, Nutricia, Nestle, GM pharma, Chr Hansen. Sanja Kolaček received fees for lectures from Abbott, AbbVie, Fresenius, Mead and Johnson, Nestle, Nutricia, Oktal Pharma. Tena Niseteo received fees for lectures from 4U Pharma. Other authors have no conflict of interest to declare. This study was part of a research project IP-2014-09-3788 funded by Croatian Science Foundation.

P-031

Regional fat distribution in children with inflammatory bowel disease: association with disease activity and phenotype

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Objectives and Study: Few studies have investigated the relationship between inflammatory bowel diseases (IBD) and body composition (BC) in children. Patients with Crohn's disease (CD) tend to have a lower lean body mass than ulcerative colitis (UC) patients. Regional fat distribution is associated with an increased long-term risk for metabolic disease. The primary aim was to assess the BC of paediatric IBD patients at diagnosis in relation with IBD phenotype and activity with an emphasis on regional lean and fat mass. The secondary aim was to evaluate the association between BC and blood inflammatory markers at diagnosis.

Methods: We performed an analysis of patients from our IBD database. Fat mass (FM), lean mass (LM) and android/gynoid ratio (AGR) were extracted from the results of dual energy x-ray absorptiometry performed within fifteen days of diagnosis. Disease activity was assessed using paediatric Crohn's disease activity index (PCDAI) or paediatric Ulcerative Colitis activity index (PUCAI). The correlations between FM, LM, AGR and disease activity were investigated using Spearman's correlation. The following blood inflammatory markers were also analyzed in association with BC: C-reactive protein (CRP), platelets, sedimentation rate and albumin.

Results: In total, 203 patients (106 males; mean(SD) age 12.8(3.0) years) with IBD (167 CD, 36 Ulcerative Colitis (UC)) were included in the study. In both groups, the interval between diagnosis and first absorptiometry were similar: CD [interval 3.0(-1.0-15.0)], UC [3.0(-1.0-14.0)] days. The mean(SD) BMI at diagnosis was 16.9(3.4) and the mean(SD) z-score of BMI was -1.2(1.6). FM and LM were lower for CD patients than for UC patients: the median(IQR) total FM was 6.7(6.8) vs 7.1(9.8) kg; total LM 26.2(9.9) vs 29.4(16.0) kg. There was no significant difference in the AGR between CD and UC: the median(IQR) AGR was 0.2(0.1) vs 0.3(0.1) respectively. In CD patients, PCDAI was not correlated with FM ($r=-0.058$, $P=0.510$), with LM ($r=-0.083$, $P=0.347$), or with AGR ($r=-0.023$, $P=0.791$). In UC patients, PUCAI was also not correlated with FM ($r=0.169$, $P=0.372$), with LM ($r=0.044$, $P=0.817$), or with AGR ($r=-0.120$, $P=0.528$). There was a variation in the FM percentage according to phenotype: mean(SD) 19(8)% for ileal; 23(10)% for colonic; 19(9)% for ileocolonic diseases. The AGR varied according to disease location: mean(SD) 0.24(0.1) for ileal; 0.27(0.1) for colonic; 0.25(0.1) for ileocolonic diseases. There was also a variation in the FM percentage in patients with extensive small bowel disease: mean(SD) 23(10)% if non-affected vs 19(8)% if affected. However, the AGR did not vary significantly: mean(SD) 0.26(0.1) if non-affected vs 0.25(0.1) if affected; $P=0.554$. As for inflammatory markers, CRP was not correlated with FM ($r=-0.100$, $P=0.405$), nor LM ($r=-0.052$, $P=0.665$). Platelet levels and albumin levels correlated moderately with fat percentage [($r=-0.31$, $P=0.008$) and ($r=0.33$, $P=0.004$) respectively].

Conclusion: IBD affecting the ileum was associated with a decrease of FM and of AGR. Regional fat distribution seems associated with disease phenotype. Thus, it is important to follow this cohort of paediatric IBD to investigate the impact of treatment on FM gain and distribution and the long-term impact on metabolic consequences.

P-032

A global prospective observational study in paediatric-onset IBD: the PIBD-SETQuality inception cohort

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Objectives and Study: The consequences of paediatric IBD (PIBD), such as growth failure, bowel resection at young age and a lifelong risk of treatment-related adverse events can have strong and lasting effects on the patient's further development and quality of life. Unfortunately we are still not able to predict which patients are at risk of developing a complicated disease course. In order to investigate this, large prospective international studies with long term follow up are needed. Currently there are no European or Asian international cohorts to compare findings during follow up within or between countries. In this first global cohort we aim to evaluate which patients are at risk based on patient and disease characteristics, immune pathology and environmental factors.

Methods: In this international prospective observational study, which is part of the PIBD Network for Safety, Efficacy, Treatment and Quality improvement of care (PIBD-SETQuality), children and adolescents diagnosed with IBD < 18 years are included at disease diagnosis. Follow up is based on a visit schedule that is in line with standard PIBD care and is intended to continue for up to 20 years. Patient and disease characteristics, as well as results of investigations, are collected at baseline and during follow up. In addition environmental factors are being assessed. In specific centres with the ability to perform extensive immunological analyses biomaterial is being collected and analysed in therapy naïve patients at baseline and during follow up. A preliminary analysis on baseline data was performed.

Results: Eighteen centres in the United Kingdom (UK), The Netherlands (NL), Italy, Israel, France, Malaysia and the United Arab Emirates are together currently recruiting over 15 PIBD patients per month. Sixteen extra centres (in 5 new countries) are preparing for their first recruitment. Since January 2017 265 PIBD patients (69% Crohn's disease (CD), 22% ulcerative colitis (UC), 9% IBDU) have been recruited which equals 29% of the target number. Patients have varied ethnicity (67.9% white; 11.1% South Asian; 2.5% black, 0.8% South East Asian; 0.4% East Asian; 0.4% Hispanic/Latino; 16.9% other or mixed race). Baseline findings are presented in Table 1.

	CD	UC / IBDU
Disease activity score (abbr PCDAI, PUCAI) n= 127 and 97 resp.	25 (IQR 15.0 – 30.0)	45 (IQR 30 – 65)
Endoscopic score (SES-CD, UCEIS) n=91 and 62 resp.	10 (IQR 6.0 – 16.0)	4.0 (IQR 3.0 – 6.0)
Type of primary induction therapy (%) n=108 and 81 resp.	66% EEN 17% prednisone 13% anti-TNF 4% 5-ASA 1% antibiotics	37% 5-ASA 63% prednisone 0% anti-TNF

Abbreviations: abbr PCDAI, abbreviated Paediatric Crohn's Disease Activity Index; PUCAI, Paediatric Ulcerative Colitis Activity Index; resp., respectively; SES-CD, Simple Endoscopic Score for Crohn's Disease; UCEIS, Ulcerative Colitis Endoscopic Index of Severity

[Table 1. Median scores at diagnosis and primary induction therapy]

Magnetic resonance enterography (MRE) findings around diagnosis were assessed in 87 patients (72% CD, n=63) and showed stricturing or fibrostenotic behaviour in 19% of those CD patients and penetrating behaviour in 3% of CD patients. The proportion of UC/IBDU patients receiving prednisone as induction therapy is higher in UK (74%, n=41) compared to NL (30% n=6), while the median disease activity score was 45 in both groups (IQR 27.5-72.5 vs. 30.0-62.5 respectively, p=0.88). Analysis of international and racial differences regarding presenting phenotype, performed diagnostics and induction therapies are ongoing.

Conclusions: As the first global inception cohort including data from European and Asian countries, this reveals valuable data on standard clinical practice and immune pathology, facilitates comparisons on diagnostic and therapeutic strategies between countries and with other national cohorts. This study enables the investigation of predictors of therapy effectiveness and provides more insight in factors associated with the risk of a complicated disease course.

P-033 (Poster of Distinction)

Pouchitis in pediatric ulcerative colitis: a multicenter study on behalf of Italian society of pediatric gastroenterology, hepatology and nutrition

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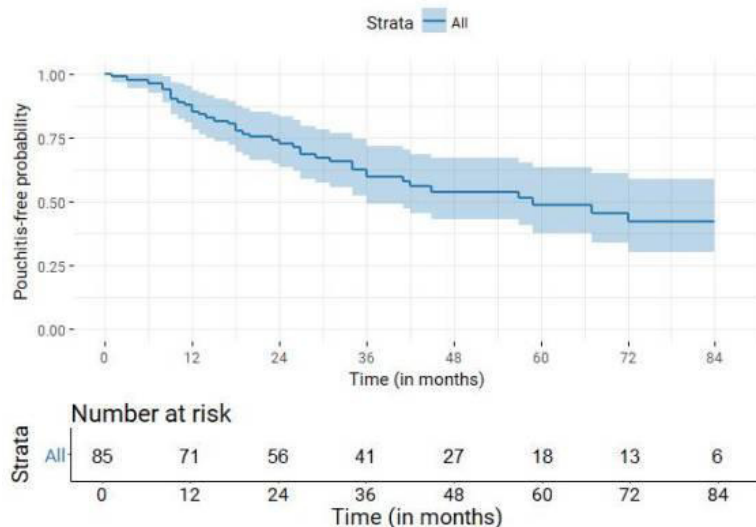
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Objectives and Study: Data on the epidemiology and risk factors for pouchitis following restorative proctocolectomy and ileal pouch-anal anastomosis (IPAA) in pediatric patients with ulcerative colitis (UC) are limited. The aim of this study was to determine incidence, risk factors and clinical outcome of pouchitis following IPAA in children with UC in Italy.

Methods: This multicenter, retrospective cohort study, included all pediatric UC patients who underwent colectomy and IPAA from January 2010 to December 2016.

Results: Eighty-five patients were enrolled. During a median post-surgical period of 24.8 (range: 1.0-72.0) months following IPAA, 38 (44.7%) patients developed pouchitis, including 6 (15.8%) who developed chronic pouchitis. Kaplan-Meier survival estimates of the cumulative probability for pouchitis were 14.6% at 1 year and 27.3% and 51.5% at 2 and 5 years, respectively (Figure). Multiple Cox regression model showed that older age at colectomy (hazard ratio, HR: 0.89, $p = 0.008$) was a protective factor, whereas chronic active colitis as indication for surgery (HR: 4.45, $p < 0.001$), and a 3-stage IPAA (HR: 2.86, $p = 0.028$) increased the risk for pouchitis. Sex, colitis extent and severity, extraintestinal manifestations, and preoperative therapeutic regimens did not affect the risk of pouchitis.

Conclusion: Long-term risk for pouchitis is significantly high in pediatric-onset UC after IPAA. Younger age at colectomy, chronic active colitis as indication for surgery and 3-stage IPAA may be considered risk factors for pouchitis.



[Figure. Overall pouchitis-free survival (\pm 95% confidence interval)]

P-034

Inflammatory bowel disease in children with elevated gamma glutamyltransferase

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Objectives and Study: The aim of this study was to assess the difference in inflammatory bowel disease (IBD) phenotype, clinical characteristics and disease prognosis among children with elevated gamma glutamyltransferase (GGT)>50U/L and primary sclerosing cholangitis (PSC)-ulcerative colitis (UC) in comparison to children with normal GGT and non-PSC, UC respectively.

Methods: Our longitudinal cohort comprised of all children diagnosed with ulcerative colitis in the province of Manitoba between 2011 and 2018. Confirmation of PSC diagnosis was based on a combination of hepatic/cholestatic biochemical markers and cholangiographic feature. Fisher exact test with bonferroni correction was used to test the relationship between categorical variables.

Results: We enrolled 190 children with IBD with 2787 person-year follow-up, of which 11 children developed PSC-IBD. The incidence rate of PSC-IBD was 3.95 per 1000 person-years. The crude point prevalence of PSC-IBD in the province of Manitoba estimated based on the 2016 Canadian census data was 3.75 per 100,000 children. Of 190 children with IBD, 95 children with UC/IBD-U with a median age at diagnosis of 14 years (IQR: 10.4-15.9y) and 1399 person-year follow-up were included. Among them, 9 children developed PSC-UC at an incidence rate of 6.43 per 1000 person-years. In this cohort, 8 (72.7%) out of 11 children with high baseline GGT, developed PSC-UC in comparison to 3 (3.6%) out of 84 children with normal GGT at baseline ($p < 0.001$). All children with high GGT at diagnosis had pancolitis in comparison to only 63.9% in the normal GGT group ($p=0.01$). Children with high GGT were more likely to be pANCA positive than those with normal GGT patients (90.9% vs. 52.0%, $p=0.01$).

Conclusions: Our findings indicated that children with UC and elevated GGT level, especially at baseline, may be predisposed to develop PSC. Children with UC should get GGT assessed at the time of diagnosis and at each clinic visit for early identification of PSC-UC.

Disclosure of Interest: This study was funded by a grant from The Childrens Hospital Research Institute of Manitoba, Winnipeg, Canada

P-035

The risk of cardiovascular complications in paediatric inflammatory bowel disease

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Objectives and Study: Ulcerative colitis(UC) and Crohn disease(CD) are chronic inflammatory bowel diseases (IBD). These diseases may promote arterial endothelial dysfunction and atherosclerosis. The problem of cardiovascular (CV) complications in IBD patients was raised in adults but paediatric data remains scarce. The aim of this pilot study was to assess the risk of cardiovascular complications in pediatric IBD with special focus on subclinical cardiovascular organic damage.

Methods: After ethical board approval we conducted a cross-sectional study in paediatric patients with IBD. We included patients older than 10 years with duration of CD or UC longer than 2 years. The exclusion criteria were: obesity, concomitant known metabolic, autoimmune or neoplastic disorder. We assessed clinical data with special focus on disease course and activity including age at the onset of disease, number of disease flares and need for surgery. Disease activity was assessed by PUCAI/PCDAI, endoscopic scoring and fecal calprotectin. Life-style evaluation was based on physical activity and dietary habits. We measured carotid intima-media thickness (cIMT), pulse wave velocity (PWV), flow-mediated dilatation (FMD) and left ventricular mass index (LVMI) as a markers of organic CV injury; lipid profiles including apolipoproteins, biochemical markers of inflammation and atherosclerosis.

Results: Fourteen patients with CD and 8 with UC were recruited to the study at the median age of 13.9 ±2.7. Most of the patient (72.7%) were in clinical remission and 18 (81.8%) received biological treatment. Fecal calprotectin was elevated in 7 patients (median 358 ug/g) BMI was < 95th percentile in all patients and none of the patients was hypertensive. In lipid profile, LDLc (117±33 mg/dL) and Lp(a) (24±20mg/dL) were significantly increased. There were no differences between CD and UC patients. PVW and LVMI were within normal range. Mean cIMT-SDS values were significantly above median of the norm but did not differ between CD (1.0(0.48-2.3) and UC (0.97-2.0) patients.FMD was abnormal in 4 patients. Most of the patients had healthy diet and proper physical activity. None of the patients experienced cardiac or thrombotic event.

Conclusions: Patients with paediatric IBD may present with increased biochemical and organic markers of cardiovascular disease. Clinical significance of these findings require further studies on bigger groups.

P-036

Serum hepcidin levels in children with inflammatory bowel disease during anti-inflammatory treatment

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Objectives and Study: Hepcidin is the central regulator of iron metabolism. Its production is mainly affected by an iron deficiency and presence of inflammatory activity in the body. The aim of this study was to compare serum hepcidin levels in paediatric patients with newly diagnosed inflammatory bowel disease and hepcidin levels during their maintenance therapy, correlate their changes with selected markers of iron metabolism and inflammation and type of provided treatment.

Methods: 43 children with newly diagnosed Crohn's disease (CD, n=30) and ulcerative colitis (UC, n=13) were included. Blood and stool samples were collected before treatment (baseline), hepcidin and haemoglobin serum levels, platelet counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin-6 (IL-6), ferritin, iron, soluble transferrin receptors and faecal calprotectin were assessed. The same parameters were measured and compared with the baseline levels in follow up period during maintenance therapy (average of 39 months after diagnosis).

Results: The CD patients had higher hepcidin levels than the UC patients at the time of diagnosis and a significant decrease during the follow-up (from 36.5 (11.5-79.6) ng/ml to 2.1 (0.9-6.7) ng/ml) was observed, while no significant hepcidin level changes were observed in the UC patients (from 5.4 (3.4-16.6) ng/ml to 4.8 (0.9-8.1) ng/ml). While hepcidin level changes correlated with disease activity and inflammatory parameters (ESR, CRP) in CD patients, they correlated only with iron levels in patients with UC. Biological therapy was accompanied by a significant decrease in CRP and IL-6 compared to conventional anti-inflammatory therapy in CD patients.

Conclusion: The higher serum hepcidin in the CD, compared to UC patients, at the onset and its higher decrease correlating with inflammatory markers reflected different contributions of iron deficiency and chronic inflammation to the anaemia development.

Acknowledgements: This study was supported by grant IGA MZ NS 9951-4 2008, IGA LF UP 2017_13, grant MH CZ-DRO (FNOI, 00098892) and by Czech Science Foundation grant GA15-13732S.

P-037

Skin symptoms in pediatric patients with inflammatory bowel diseases

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Objectives of Study: Inflammatory bowel diseases-IBD are systemic inflammatory diseases, affecting mainly the gastrointestinal system. Extraintestinal manifestations occur frequently. Skin symptoms are specific or reactive part of systemic inflammation, therapeutic adverse events or independent of the bowel disease.

Materials and methods: Authors present the skin complications of IBD between years 1998 and 2018. 246 patients suffering from IBD were treated in Department of Pediatric Gastroenterology, Pediatric Health Centre of Borsod-Abaúj-Zemplén County Central University Hospital, Miskolc, Hungary. 76 of patients were followed between 1998-2008, 170 between 2009-2018. The objective was to determine the incidence of different skin disorders in the patient-group treated in two different decades by retrospective way using paper form and electronic medical records.

Results: 48 of 76 patients of 1st decade (63.1%) had Crohn disease (CD), 4/76 (5.2%) indeterminate and 24/76 (31.6 %) ulcerative colitis (UC). 34 patients had dermatoses and/or stomatitis associated with bowel disorder. Some of the patients had multiple mucocutaneous manifestations. Occurrence of IBD specific skin complications (fistules, fissures, periorifital inflammation) was 18/76 (23%), 16/48 in Crohn disease (33.3%), 2/24 in ulcerative colitis(8.3%). Association with dermatoses based on similar or same pathogenesis-reactive symptoms (pyoderma gangrenosum, with, or without micro and macropustules, necrotizing panniculitis, erythema nodosum, vasculitis-like lesions, oral mucous membrane ulcers, alopecia areata, Raynaud phenomenon, skin signs of thromboembolic complication) occurred in 12/76 (14.5%) patients. Consequences of immunosuppressive therapy (steroid acne, striae cutis, hypertrichosis, bacterial, mycotic, viral infections) developed in 16/76 cases (21%). Skin changes, independent of IBD were not discussed. Only one reactive skin disease, erythema nodosum occurred as part of systemic inflammation in group of 170 patients, followed in the second decade. Other types of skin manifestations were not examined in this group. Authors used routinely biologics for therapy during the second decade. The most serious problems accompanied Crohn disease.

Conclusion: Skin symptoms appearing before and at the appearance- time of gastrointestinal signs can be helpful in establishing diagnose and planning systemic therapy. Biologics are helpful in minimizing the systemic inflammation.

P-038

Oral and periodontal manifestations in Paediatric Inflammatory Bowel Disease

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Objectives and Study: Oral and periodontal involvement is a frequent extraintestinal manifestation in Pediatric Inflammatory Bowel Disease (PIBD) observed in 50 to 80% of patients. Our aim is to know the prevalence of these manifestations in our PIBD cohort and to evaluate their salivary characteristics.

Methods: Descriptive study of the oral and periodontal manifestations of PIBD patients followed in our PIBD Unit. Patients were offered a dentistry evaluation at the onset of the disease or during the follow-up from November 2018 to February 2019. Medical data was recorded from clinical history and a dental examination was performed by the same examiner. To measure the pH (normality 7-7.4) and stimulated salivary volume (normality 6ml / 5 ´) the Saliva Check Buffer® test was used.

Results: Thirty-five patients were included (mean age: 13 years (range 8-18), 46% males). Nineteen patients (54.2%) had Crohn's Disease (CD), 15 (42.8%) Ulcerative Colitis (UC) and one patient (2.8 %) IBD unclassified (IBDu). Seventy-four percent of patients were evaluated during follow-up (60% remission, 14.2% with active inflammation) and 25.7% at disease onset. Seventy-four percent of CD patients were under biological treatment (associated with immunomodulators in 52,6% of them). Salicylates were used in 73,3% of UC patients. Oral manifestations diagnosed in the buccal mucosa were: cleft lips 37% (n = 13), oral ulcers 8.5% (n = 3), leukoplakia 3% (n = 1) and geographical tongue in 3% (n = 1). Globally, 57% of the patients had moderate gingivitis, without differences regarding the stage of the disease (onset, active disease in the follow-up, or remission). At the dental level, 17.5% (n = 6) of the patients were affected by molar incisor hypomineralization. From the overall sample, 16 patients presented a basic salivary pH (9 EC - 7 CU), 13 acid pH (8 EC - 5 CU) and 6 normal pH. Regarding the total volume of stimulated saliva, the values were normal (8.2ml EC and 7.3ml CU).

Conclusion: In this preliminary study of oral manifestations in a cohort of pediatric IBD patients, moderate gingivitis was found to be the most prevalent periodontal condition. There is a wide variability of salivary pH, but with normal volumes of saliva after stimulation tests.

P-039

Epstein-Barr virus serological status in paediatric patients with inflammatory bowel disease

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Objectives and Study: The impact of Epstein-Barr virus (EBV) infection on the clinical outcomes of children and adolescents with inflammatory bowel disease (IBD) is not well known. The aim of the study is to evaluate the seroprevalence, seroconversion rate and complications associated with EBV infection in a cohort of paediatric IBD patients at a tertiary care hospital.

Methods: a descriptive study was performed collecting demographic, clinical and treatment data from medical records as well as EBV serological status of paediatric IBD patients from 2012 to 2018. In seronegative patients, seroconversion rate was evaluated. Complications associated with primary EBV infection were described. From September 2016, EBV serology was included into the initial work-up for IBD patients. For those patients who did not have EBV study at IBD onset, it was performed during follow-up.

Results: A total of 307 patients with IBD were diagnosed between 2012 and 2018. EBV status was available from 131 (43%). Of those patients 57% had Crohn's Disease, 41% Ulcerative Colitis, and 2% IBD unclassified (66% males; median age at IBD diagnosis: 13.2 years (IQR: 0.8-17.8)). In 102 patients, serological EBV status was determined at IBD onset; while in 17 patients it was performed during the follow-up. Overall EBV seroprevalence was 67%, and no differences were observed regarding age (over or under 10 years-old). EBV seroprevalence was higher in females than in males (80% vs. 60.5%, $p=0.02$). Regarding IBD treatment, 84% had received immunosuppressive treatment [thiopurines (32%), anti-TNF (9%) and combined treatment (59%)], without differences in the seroprevalence rate according to the treatment modality. Forty-three patients were seronegative, and 12 of them had a second determination during follow-up. Overall, 5 patients showed seroconversion (42%) after a mean follow-up of 24 months (IQR: 22-26). All these patients had received treatment with thiopurines: 2 patients presented a symptomatic mononucleosis with neutropenia, requiring hospital admission and withdrawal of immunosuppressive treatment and 3 patients had asymptomatic primary infection.

Conclusion: EBV seroprevalence in our paediatric IBD cohort is similar as previously described in the literature. EBV status study in patients with IBD, especially prior to initiation of thiopurines, may be useful to plan subsequent follow-up since a non-negligible percentage of them could present with complications of primary EBV infection under immunosuppressive treatment.

P-040

EBV status and seroconversion rate in children with IBD

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Objectives and Study: Inflammatory bowel disease (IBD) requires consistent and often lifelong immunomodulatory therapies including corticosteroids, azathioprine, methotrexate or different biologicals. A primary infection with Epstein Barr virus (EBV) under immunosuppression, particularly thiopurins, has been reported to be associated with an increased risk for the development of a hemophagocytic lymphohistiocytosis (HLH), (*Hyams et al Gastroenterol 2017;152:1901-14*). Data on EBV status in children with IBD are scarce. The aim of this study is to determine the prevalence of positive EBV serology and seroconversion rate in children with IBD.

Methods: The study cohort included all children with IBD who were diagnosed and/or treated in our center from 2003 to 2019. Clinical information on age, gender, type of disease, therapies, and EBV status at diagnosis were retrospectively extracted from the charts and were prospectively performed during the course of the disease. Seronegative patients were included in the prospective arm of the study and if required, a current EBV serology was determined.

Results: Of 404 included patients, EBV serology had been performed at the time of diagnosis in 183 subjects (Crohn's disease, ulcerative colitis and IBD-U in 98, 73, and 12 patients, respectively, 45% females, mean age \pm SD 11.0 ± 3.9 years). EBV-naïve children (n=86, 47%) were on average 1.4 years younger (10.6 ± 4.2) than EBV positive patients (12.0 ± 3.6), ($p = 0.02$). IBD diagnosis and gender did not affect the EBV status. In 56 (65%) seronegative subjects with available follow up serology, seroconversion was proven in 8 (16%) after a mean follow up time of 4 ± 3 years. Nine of 11 children reached the age of 18 years still being EBV-naïve. Patients exposed to azathioprine (n = 25) had a 2.5-fold increased risk of seroconversion compared to azathioprine naïve patients. One EBV-seronegative patient treated with azathioprine and infliximab was diagnosed with Hodgkin's disease at the age of 17 years.

Conclusion: Almost 50% of the paediatric patients in our cohort were EBV-naïve at diagnosis. EBV seroconversion during the course of the disease was low (16%) and theoretically put EBV-naïve patients at an increased risk for HLH. The use of thiopurines should be critically discussed in EBV-naïve children and adolescents with IBD.

P-041

A decade of Varicella and EBV screening within a paediatric inflammatory bowel disease population: good rates of detection but room for improvement in post varicella vaccination immunity status

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Objectives and Study: Varicella (VZV) vaccination is not part of the routine immunisation schedule in the UK. We aimed to evaluate the impact of the VZV screening and immunisation programme within the paediatric inflammatory bowel disease (PIBD) population at a tertiary paediatric centre over a 10-year period (2009-2018). Additionally we aimed to record the EBV screening programme over an 8-year period (2011-2018).

Methods: Data regarding IBD diagnosis, age at diagnosis, VZV and EBV testing and status were collected retrospectively from a departmental database and patient records (electronic and paper notes).

Results: 520 patients were diagnosed with IBD within the study period (2009-2018) with a median age at diagnosis of 12.5yrs (IQR 4.2). 503/520 (96.7%) were tested for VZV status, with 45/503 (8.9%) confirmed to be VZV naïve. Median age of the VZV naïve cohort was significantly lower at 8.2yrs (vs 12.8yrs within the VZV immune cohort ($p < 0.00001$)). 22/45 (48.9%) VZV naïve patients were documented to be immunised, of which 5/22 (22.7%) had subsequent confirmation of sero-conversion (2 in progress). 2/23 (8.7%) unimmunised children were documented to require post-exposure prophylaxis and 2/23 (8.7%) required active treatment for VZV during the study period. Inability to vaccinate due to immunosuppressant medications was clearly documented in 6/23 (26.1%). Of the 437 patients diagnosed with IBD between 2011 and 2018, 407 (93.1%) were tested for EBV. 190/407 (46.7%) were EBV naïve. The median age of EBV naïve patients was not significantly lower than those who had previous exposure to EBV (12.4yrs vs 13.1yrs, $p=0.10$).

Conclusion: We demonstrate high rates of VZV and EBV testing within our PIBD population. Vaccination of VZV naïve patients is taking place, however potential for improvement in establishing a patients immunity status following immunisation has been highlighted with this study.

Disclosure of Interest: LC - conference fees - Ferring, Tillots. VG - speaker's/conference fees - Ferring, Abbvie. LG - research consultancy session - Lilly R Hansen - speaker's fees, travel support, and/or participated in medical board meetings - MSD Immunology, Dr Falk, Nutricia, 4D Pharma. RKR - speaker's fees, travel support, and/or participated in medical board meetings - Nestle, MSD Immunology, AbbVie, Dr Falk, Takeda, Napp, Mead Johnson, Nutricia, 4D Pharma. Remaining authors: nil competing interests declared.

P-042

Prevalence of food allergy in children with inflammatory bowel disease in Ireland

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Objectives and Study: There has been a rapid increase in the number of children with both inflammatory bowel disease (IBD) and food allergy (FA) in recent times. Many shared factors have been implicated in the aetiology of both conditions including diet, breastfeeding, antibiotics and a hygienic environment. It is believed that these factors affect the infant's gut microbiome and hence their developing immune system. The aim of this study is to report the prevalence of ever having an IgE mediated FA in children with IBD in Ireland. We hypothesised that the prevalence of ever having a FA in children with IBD is different to the prevalence in Irish children (4.5%) as reported in the literature.

Objectives:

1. To identify all children diagnosed with IBD in Ireland during the study period.
2. To determine the prevalence of FA in children with IBD.
3. To determine if there is a difference in the prevalence of FA in children with CD versus UC.

Methods: A prospective observational study was done in the National Centre for Gastroenterology, Our Lady's Children's Hospital, Crumlin, Dublin, Ireland. It included all children 0-17 years diagnosed with IBD in the Republic of Ireland over a 26-month period (December 2016- January 2019). Data was collected by questionnaire with and questions relating to FA were designed by specialists to ensure a current or previous history of IgE mediated FA was captured.

Results: There were 209 children diagnosed with IBD over 26 months giving an unadjusted incidence of 8.8 per 100,000 children per year. Twelve of these children were considered to have IgE mediated FA which equates to a FA prevalence of 5.7% (95% CI 3.3 to 9.8). The odds of having FA in the setting of childhood UC is 1.73 times greater than with childhood CD (95% CI: 0.51 to 5.82).

Conclusions: We report a marginally higher prevalence of ever having a FA in children with IBD when compared to children without IBD as reported in the literature. Further longitudinal research is necessary to confirm this association and understand the mechanisms underlying it.

Fatigue in paediatric IBD: a multicenter case-control study

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Objectives and Study: Fatigue and decreased physical fitness are common findings in children and adolescents with inflammatory bowel disease (IBD). Explanatory factors at times of severe active inflammation may be anaemia, weight loss and disturbed sleep, yet the causes of fatigue in clinically quiescent or moderately active paediatric IBD have been inadequately studied.

Methods: We conducted a case-control study of 106 children and adolescents with quiescent to non-severe IBD (defined as Paediatric Ulcerative Colitis Activity Index (PUCAI) scores below 65 and Paediatric Crohn's Disease Activity Index (PCDAI) scores below 30). They were recruited from 5 tertiary care and 6 secondary care centres in Belgium and the Netherlands. Cases (n=23) were patients who scored 2 standard deviations (SD) below the age specific mean of the PEDSQL fatigue scale, and controls (n=83) had scores above this cut-point. Higher scores on the PEDSQL fatigue scale indicate fewer symptoms of fatigue. Causal factors of fatigue previously associated with severe disease activity were studied.

Results: Out of the total study cohort, 77 patients (73%) had Crohn's disease (CD), 25 (24%) had ulcerative colitis (UC) and 4 (4%) had IBD-unclassified. The proportion of fatigued patients per phenotype was not different (CD 23% vs. UC 20%, p=0.821). The mean six-minute walking distance, an established method to assess exercise capacity, was not different between cases and controls (respectively -1.10 vs. -1.04 SD, p=0.863), and neither was the haemoglobin level (respectively -1.7 vs. -1.5 SD, p=0.589). The proportion of patients that were not in clinical remission was significantly higher in cases compared to controls (63% vs. 27%, p=0.003), but the proportion of patient with out-of-range faecal calprotectin values (>250 mg/g) was not different (respectively 55% and 53%, p=0.928). The disease-related quality-of-life score (IMPACT-III) was significantly lower in cases compared to controls (respectively 123 vs. 146, p< 0.0001).

Conclusion: Irrespective of how children and adolescents with IBD scored themselves on the PedsQL scale, both cases and controls are more fatigued than their healthy peers and have a reduced exercise capacity. Cases as well as controls have lower haemoglobin levels than their healthy peers, but there is no difference between them. Patients who scored themselves as fatigued, also had higher clinical activity scores and lower quality-of-life scores. Fatigue in paediatric IBD is likely to be related to a combination of biological, functional and behavioural factors. All of these factors should be taken into account when managing the fatigued child with IBD.

P-044

Incidence and characteristics of rare and severe complications in children with paediatric-onset IBD; the international PIBD SETQuality safety registry by PIBDnet

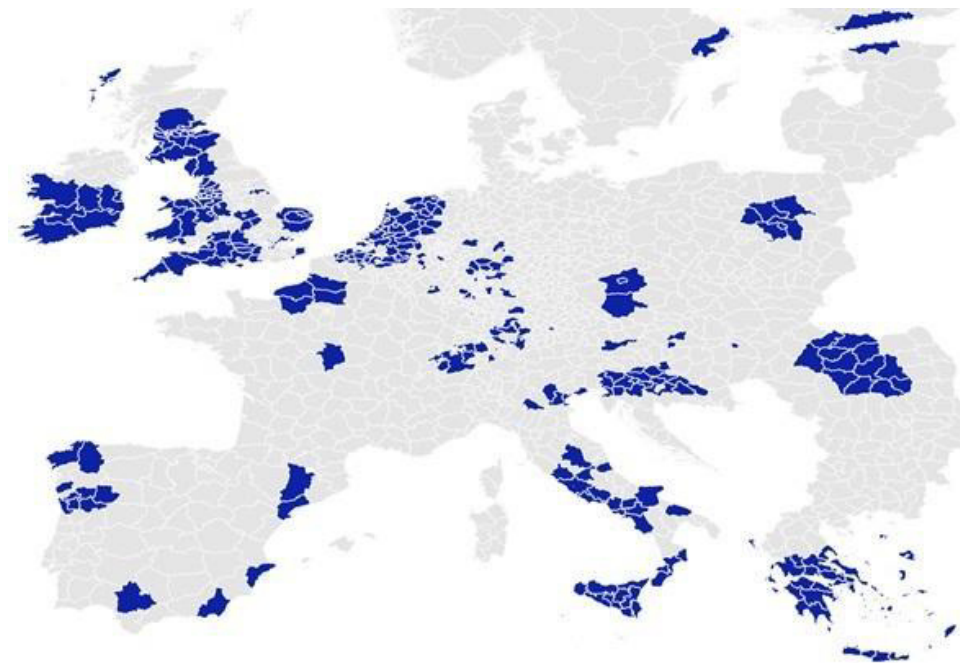
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Objectives and Study: Paediatric-onset IBD (PIBD) patients often present with more serious disease than adults and are exposed to intensive treatment, which may lead to rare but very severe complications. Due to the rarity of these events available data is limited, resulting in prevention and treatment recommendations based on very low evidence or even absence of any recommendations. Therefore an international study is essential to obtain data on the incidence and to characterize these complications. With this safety registry for rare and severe complications in PIBD we aim to improve knowledge on incidence and risk factors of rare and severe complications.

Methods: Paediatric gastroenterologists in 26 different countries reply to a monthly email to indicate whether they have seen one of 10 complications in an IBD patient < 19 years. This list of predetermined complications was established with input from the PIBD-SETQuality consortium and the paediatric IBD Porto group of ESPGHAN. The survey also enables the physicians to report any 'other' complication that is rare and severe in their opinion. Information regarding patient- and disease characteristics, previous therapies and the specific complication is collected for each registered complication. Additionally, participating physicians annually report the number of new and current PIBD patients under their care. The calculation of the incidence per country and region is based on validated population statistics from Eurostat and the Poisson distribution for rare events.

Results: In this ongoing registry 150 paediatric gastroenterologists are currently participating. Since the start of this registry in October 2016 response rate has increased to currently over 110 responses per month, resulting in an overall response rate of 80%. Based on the first two year's annual reports the estimated current covered population comprises 32 million children and adolescents including 9000 PIBD patients. In Europe in particular the covered children and adolescent population comprises 29 million (Figure 1).



[Figure 1. Covered European regions as defined by Eurostat 2013 based on the current participants]

A total of 85 categorized complications were reported. Opportunistic infections (n=17) and renal failure (n=16) were most frequently reported, followed by severe sepsis (n=13), venous thromboembolism (n=12) and cancer (n=9). Death (n=5) and bone marrow failure (n=5) were reported less frequently. The remaining reported cases were severe neurological disease (n=3), hemophagocytic lymphohistiocytosis (n=3) and liver failure (n=2). In addition 38 reports described a rare but severe complication outside these categories. No new categories could be established based on these other complications. Preliminary findings show an overall incidence of any of the listed complications of 6.7 per 1000 PIBD patients annually (95% CI 5.0-8.7).

Conclusions: Over a 2.6 year period 123 rare and severe complications in PIBD patients were prospectively identified, resulting in an annual incidence of 6.7 per 1000 PIBD patients. Besides the identification of a variety of severe adverse events, this enables understanding possible causes, management and outcomes of rare but severe events in PIBD. Moreover, this may enable prevention of these events.

P-045

Increased chance of acute pancreatitis in patients with inflammatory bowel disease - a meta-analysis

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Objectives and Study: Inflammatory bowel disease (IBD) may be associated with several extraintestinal disorders making the disease burden even higher. Clinical experience shows, that acute pancreatitis (AP), which is a potentially life-threatening disease, occurs more often in patients with IBD. Our current knowledge on this association is, however, very limited. Therefore, we aimed to systematically explore, analyse and critically appraise all the currently available literature on this topic and to conduct a meta-analysis.

Methods: We conducted a systematic search on the online databases of PubMed/MEDLINE, EMBASE, SCOPUS, Web of Science and Cochrane Library from inception to 30th October 2017. Case-control and other observational studies (cohort and randomized trials), reporting the occurrence of AP in an IBD population of any age, were included. Filters for “English” and “human” were applied. All stages of screening and data extraction were conducted by two reviewers independently. Pooled analyses were performed using random effects model.

Results: After screening 2679 entries of the database search, a total of 170 studies were included in this meta-analysis. Eight of the 170 publication (including 186 755 patients) were case-control studies reporting ORs of AP in IBD. The other 162 cohort and RCT studies that reported the events of AP among IBD patients. Pooled OR of AP in IBD was found to be 3.22 (95% CI: 2.61-3.97; I²: 62%). An AP episode was seen in 1,74% (95% CI: 1.43%-2.07%; I²: 87.28%) of the overall IBD population of the 162 studies (data of 115 539 patients). AP occurred in 2.96% of patients taking thiopurine medications, while this number was 0,35% in those, who did not take thiopurines (p< 0.01). We found no significant differences in the event rates between IBD subtypes, genders and age groups (children vs. adults).

Conclusion: We have searched the currently available literature, and based on our pooled analysis the odds of AP in IBD is 3 times higher than in the general population. There is data that shows, the majority of these events may be associated with thiopurine treatment. To more extensively explore the aetiology, clinical behaviour and prognosis of the IBD associated AP, further clinical and pathophysiological studies are needed.

P-046

The risk of cancer and mortality in paediatric onset inflammatory bowel disease in Denmark and Finland during a 23-year period: a population-based study

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Objectives and Study: Recent studies report increased risks of both cancer and mortality in paediatric onset inflammatory bowel disease (pIBD) but the reproducibility of this is unknown. In this population-based study we aim to estimate the risk of cancer and mortality in the Danish and Finnish pIBD population in a 23-year period compared to the general population.

Methods: The pIBD population was defined as individuals registered in the national patient registries with a diagnosis of Crohn's disease (CD), ulcerative colitis (UC) or IBD-unclassified before their 18th birthday from 1992-2014. This cohort was cross referenced with the national cancer and mortality registries identifying all pIBD patients who subsequently developed cancer and / or died and followed up to the end of 2014. Risk estimates are presented as standardized incidence ratios calculated based on incidence figures from the populations.

Results: 6,689 patients with pIBD were identified (median age at follow-up 22.3; median follow-up: 9.6 years (interquartile range: 4.8-16.0)). 72 subsequently developed cancer and 65 died. The standardized incidence ratio of cancer in general was 2.6 (95% confidence interval (CI): 1.8-3.7) and 2.5 (95%CI: 1.8-3.4) in CD and UC, respectively. The standardized mortality ratios were 2.2 (95% CI: 1.4-3.4) and 3.7 (95% CI:2.7-5.0) in CD and UC, respectively. The leading causes for mortality were cancer, suicide and infections.

Conclusions: We found an increased risk of cancer and mortality in pIBD. This underlines the importance of cancer surveillance programs and assessment of mental health in the standard of care in adolescent pIBD patients.

P-047 (Poster of Distinction)

Safety and efficacy of ferric carboxymaltose [FCM] for the treatment of iron deficiency anaemia in paediatric patients affected by inflammatory bowel disease (pIBD)

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Objectives and Study: Iron deficiency anaemia (IDA) is common in pIBD affecting cognitive development and quality of life, and its oral treatment is hampered by poor compliance and efficacy. Intravenous FCM has been shown to be effective and safe for IDA in adult patients, but paediatric studies are limited. We aimed to study the safety and efficacy of FCM in the treatment of IDA in pIBD.

Methods: Retrospective review of all pIBD patients with IDA treated with FCM between 2013 and 2018 in two tertiary care paediatric IBD centres. IDA was diagnosed by combining haemoglobin (HB), haematocrit (HCT), mean cell volume (MCV), iron levels, and ferritin. Inflammatory biomarkers (C-reactive protein [CRP], faecal calprotectin [FC]) and phosphate levels were also assessed. Patients received 15 mg/kg of FCM (total weekly dose max 500 or 1500 mg according to body weight < or > 35 kg respectively). Bloods were repeated 4-6 weeks and 12 weeks after each infusion. Concomitant medications, changes in treatment (dose escalation/shift to different drugs), disease activity measured by Physician Global Assessment (PGA) and PUCAI or PCDAI were recorded at same time points.

Results: A total of 203 infusions were administered to 128 pIBD patients with IDA, 68 males (53.1%), Crohn's disease = 88 (68.7%), ulcerative colitis = 23 (17.97%), inflammatory bowel disease unclassified = 17 (13.3%). Overall, a total of 186 infusions were analysed for sustained efficacy as 17 were excluded because of an additional infusion needed within 12 weeks from the previous one. Mean age at the first injection was 12.46 years (SD 3.63, range 3-18). The mean number of weeks between infusions for patients requiring multiple infusions (n=44) was 34.74 (SD: 34.20). Relevant changes in concomitant medications were needed at the time of 101/186 infusions (54.3%). Four-six weeks after FCM injection, a significant improvement was found in HB (106.36 ± 16.518 vs 122.73 ± 12.835 , g/L $p < 0.001$), MCV (74.424 ± 10.123 vs $80.602 \text{ fL} \pm 22.244$, $p < 0.001$), iron (6.060 ± 3.982 vs 11.737 ± 6.829 $\mu\text{mol/l}$, $p < 0.001$), ferritin (67.29 ± 109.467 vs 218.15 ± 212.387 $\mu\text{g/L}$, $p < 0.001$) and ESR (32.92 ± 26.82 vs 25.99 ± 22.98 mm/hr, $p < 0.05$). Furthermore, 12 weeks after the FCM infusion a significant statistical difference compared to baseline was found in the following parameters: HB (107.32 ± 15.331 vs 123.74 g/L ± 14.646 , $p < 0.001$), MCV (74.851 ± 10.224 fL, $p < 0.001$), iron (6.527 ± 3.959 vs 10.463 ± 6.4528 $\mu\text{mol/L}$, $p < 0.001$), ferritin (80.27 ± 146.183 vs 137.07 ± 146.466 , $\mu\text{g/L}$ $p < 0.05$). There was no statistically significant difference for CRP and FC at week 0, 4-6 and 12 (repeated measures). The interaction effect of the disease phenotype and changes in treatment on the outcome (level of Hb at week 4-6 and 12) was not statistically significant. Only 3 patients reported an adverse reaction; one developed an anaphylactic reaction, the remaining 2 pruritus and transient fever. Among the 25 patients with low serum phosphate, only 2 had the severe hypophosphatemia (phosphate ≤ 0.3 mmol/L) requiring correction. No adverse events were recorded in patients under 6 years old ($n = 11$).

Conclusion: FCM administration is safe and effective for routine management of IDA in children with IBD, including those who are under 6 years old.

P-048

Improvement of health related quality of life in children with inflammatory bowel disease receiving routine intravenous iron supplementation

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Objectives and Study: Iron deficiency anemia (IDA) is very common in children with inflammatory bowel disease (IBD). While health related quality of life (HRQL) is a key outcome measure, no long-term studies have evaluated the effect of correction of IDA on HRQL in children with IBD. The objective of this study was prospective evaluation of changes HRQL in iron deficient children with IBD receiving routine iron supplementation with periodic intravenous iron sucrose (IVIS).

Methods: 38 children with IBD, treated with infliximab participated. Hematology and inflammatory markers were assessed before each infliximab treatment. Iron deficient patients (transferrin saturation below 20% and/or ferritin below 30 ng/ml or 100 ng/ml with normal or elevated C-reactive protein, respectively) received IVIS after each infliximab infusion until iron indices stayed normal for two consecutive measurements. HRQL was assessed with Pediatric Quality of Life Inventory every 4 months. Correlation between changes in mean hemoglobin levels and HRQL scores was analyzed prospectively in 3-month periods over a period exceeding 3 years.

Results: At enrollment, 27 patients had already been established on infliximab; 11 had not started or completed induction. Mean iron indices and hemoglobin normalized after 3 and 6 month of starting IVIS, respectively. Multiple HRQL parameters significantly improved, regardless of the duration of infliximab treatment at the time of enrollment. There was statistically significant positive correlation between correction of anemia and improvement in parent-reported emotional and physical HRQL scores.

Conclusions: Periodic IVIS resulted in long-term correction of IDA in children with IBD. Correction of IDA contributed to improvements in HRQL.

P-049

Use and efficacy of enteral nutritional therapy as maintenance of paediatric Crohn's disease; analysis of Japanese nationwide registry

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Objectives and Study: Enteral nutrition (EN) is used as an effective treatment for active Crohn's disease in children. In Japan, most of paediatric gastroenterologists recommends supplemental enteral nutrition as a maintenance therapy. However, efficacy of EN as a maintenance therapy is unclear. We have analyzed Japanese multicenter registry data to evaluate the use and long-term efficacy of EN as a maintenance of paediatric Crohn's disease.

Methods: Twenty-five hospitals in Japan has joined to the registry. Newly diagnosed paediatric IBD patients between 2012 and 2018 were registered to the study. The treatment received, which were prospectively recorded every 6 months since onset were analyzed.

Results: Data of patients whose details of treatment at every follow up period was registered were extracted from registry. Among 115 patients, 110 (96%) patients have received EN at any time of the treatment. Forty-two (38%) received exclusive enteral nutrition, and 106 (92%) received supplemental enteral nutrition. All but 2 patients were treated with elemental formula. Among 47 patients started treatment with EN alone, 11(23%) maintained remission without steroids, immunomodulators or biologics (median follow up period 1.5 years, range: 0.5-5.0 years).

Conclusion: EN is widely used among Japanese paediatric Crohn's disease patients. Most of them are treated with elemental formula. Although lack of controlled study compared with patients without EN, supplemental enteral nutrition seems effective in avoiding steroids and biologics use in some patients.

P-050

Nutritional and bone mineralization status in paediatric Crohn's disease patients: does exclusive enteral nutrition help?

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Objectives and Study: Pediatric patients affected by Crohn Disease(CD) have an increased risk for low catch-up growth and bone mineralization disorders, due to the chronic inflammation, the malnutrition, and the malabsorption of nutrients. Our aim was to investigate the impact of Exclusive Enteral Nutrition(EEN) on the body composition, nutritional status, and bone mineral density(BMD) in a cohort of pediatric CD patients.

Methods: CD newly diagnosed patients were prospectively enrolled. At the time of diagnosis(T0), at 8 weeks(T8), at 26 weeks(T26), and after 52 weeks(T52) from the diagnosis, a complete physical evaluation was performed together with blood vitamin measurements. The Fatty Free Mass (FFM) and the Resting Energy Expenditure (REE) were measured through the use of Bioelectrical Impedance (BIA). Moreover at T0, T26 and T52 a dual-energy X-ray (DXA) was performed to assess patients' BMD. The BMD of CD patients was compared by using the data obtained in a healthy control population sex and age matched to our patients, derived from the same geographical area using the same DXA device.

Results: Eighteen consecutive CD pediatric patients were enrolled in the study. The median age was 13 years (range: 8-16). Fourteen out of 18 were males (77.8%). All patients started EEN as remission induction therapy. Children with CD had a significant lower BMD compared to healthy controls ($p < 0.001$) both at T0 and after one year ($p = 0.00042$). The BIA analysis showed a significant increase at T26 and T52 of FFM ($p = 0.023$ and $p < 0.001$) and of REE ($p = 0.011$ and $p < 0.001$). We also found statistically significant correlations between FFM measured by BIA and height z-scores, and REE at T0 ($r = 0.703$ - $p = 0.001$ and $r = 0.870$; $p < 0.001$ respectively) and T52 ($r = 0.780$ - $p = 0.0001$; $r = 0.902$ - $p < 0.001$ respectively). BIA and DXA used for measurement of FFM had a high agreement at T0 (CCC=0.958; 95%CI [0.896;0.984]) and at T52 (CCC=0.428; 95%CI [0.044;0.701]). Finally there was a significant correlation between FFM measured by BIA and BMD measured by DXA at T0 ($r = 0.542$ and $p = 0.025$), at T26 ($r = 0.637$ and $p = 0.019$) and at T52 ($r = 0.532$ and $p = 0.041$). There was also an improvement of the z-score for the weight, the height, the Body Mass Index (BMI), and the tricipital skinfold thickness. Moreover, there was a significant reduction of PCDAI, erythrocyte sedimentation rate, platelet count, and ferritin and an improvement of 25OH vitamin D, vitamin A, vitamin B12, and folates blood levels at all time points during the EEN.

Conclusions: EEN improves bone mineral composition and the FFM and REE, leading to the improvement of the basal metabolism rate. Moreover, EEN improves the nutritional status in CD children by increasing serum vitamin levels and restoring the patient's physical state through an increase of weight, BMI, and tricipital skinfold thickness. Finally, in our cohort of patients, the FFM is also directly related to BMD. Even if further studies are needed, our data suggests that FFM measured by BIA could represent a safer and indirect measure of children bone metabolism.

P-051

Maintenance of remission after treatment with exclusive enteral nutrition and Azathioprine in patients with Crohn's Disease

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Objectives and Study: Several studies have shown the efficacy of Exclusive Enteral Nutrition (EEN) in patients with Crohn's Disease (CD) for the induction of remission. ECCO-ESPGHAN guidelines recommend the use of EEN combined with early use of immunosuppressants in paediatric patients with mild to moderate CD. However, there is a lack of data to show its efficacy in the long term to avoid or postpone the use of biological treatment. The aim of our study is to know how many of our patients that have achieved remission with EEN and Azathioprine (AZA), required to step up to biological treatment during the follow-up.

Methods: Retrospective analysis of paediatric patients with CD that were diagnosed at our Unit between 2003 and 2017. We included those patients that achieved clinical remission after treatment with EEN and AZA. We analyse demographic, clinical and follow-up data until February 2019 or until they are transfer to an adult Inflammatory Bowel Disease (IBD) unit.

Results: We included 91 patients (68.1% males; Mean age at onset: 12.29 years and median of 13 years old, range 8 months-17 years old). Mean time of follow-up was 60.45 months (range: 8-165 months). During this period, 66/91 patients (72.5%), had a flare. Seventeen of those patients (20.2%) received a second cycle of EEN, being effective in 7 (41.2%). Mean time from diagnosis until the second cycle of EEN was 13.76 months (maximum: 110 months). Globally, 64.8% of our patients required to step up to biological therapy. Mean time from onset to biologics was 15.3 months (median 9 months). Seventy two percent of those who needed biological treatment started Adalimumab (ADA). During the follow up, 42.2% of the patients with combo therapy could withdraw AZA, being the main reason (76.3%) clinical and endoscopic remission.

Conclusions: Even though EEN is an effective treatment for the induction of the remission in paediatric CD, in the long term we are not able to maintain that remission and an important percentage of patients require to step up to biological therapy. The definition of more strict criteria of remission is necessary in order to establish the most suitable maintenance treatment for each patient.

P-052 (Poster of Distinction)

Exclusive enteral nutrition versus corticosteroid induction therapy for new onset paediatric Crohn's disease: comparison of 18 month outcomes in a Canadian prospective multi-centre inception cohort

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Objectives and Study: Exclusive enteral nutrition (EEN) is successfully used as initial therapy of new onset paediatric Crohn's disease (CD), but long-term benefits in comparison to the alternative of short-term corticosteroid (GCS) induction have seldom been assessed.

Methods: Beginning April 2014, children aged 2 to 17 years presenting with new onset Crohn's disease (CD) to one of 12 Canadian academic paediatric IBD centres have been systematically evaluated according to Porto guidelines and prospectively enrolled in an inception cohort study of the Canadian Children IBD Network (CIDsCaNN). Comprehensive baseline and longitudinal data are prospectively recorded. All those receiving EEN or GCS as their initial therapy and under follow-up for a minimum of 18 months were included. Propensity score methodology was used to balance the exposure groups. Outcomes and subsequent treatment exposures were interrogated using logistic regression and cox proportional hazards models.

Results: Between April 2014 and April 2017 344 (53%) of all children with CD (56% Male) median age 13yrs (IQR: 11.1-14.7yrs) commenced either EEN (55%) or GCS (45%) as their first induction therapy for luminal CD. EEN-treated and GCS-treated patients were similar at baseline with respect to age, gender, linear growth, weight z-score and serum inflammatory markers. Patients initiated on GCS had a marginally greater baseline disease activity (Mean wPCDAI 64 vs 57, $p = 0.04$). Patients with isolated colonic disease were less likely to be initiated on EEN (OR 0.39, $p = 0.002$). Immuno-modulator maintenance therapy initiation within 90 days (51%) and disease activity at 6 months (Remission 51%; Mild 25%; Mean wPCDAI 15 +/- 18) were identical between the groups. Of patients initiated on EEN, 9/190 (5%) went on to commence steroids within 60 days. Ongoing/subsequent steroid exposure was greater in the GCS group (6mths: 8%; 12mths: 7%; 18mths: 5%) than the EEN group (6mths: 4%, 0% thereafter). Whilst anti-tnf therapy initiation within 90 days was similar between groups (EEN: 27%; GCS 34%; $p = 0.16$), it was slightly greater in the GCS group by 18 months (EEN: 59%; GCS 69%; log-rank $p=0.09$). Surgical resection by 18mths was similar (EEN: 5.2%; GCS: 4.5%). Linear growth during 18 month follow-up was similar (mean delta Ht z-score EEN: 0.09; GCS: -0.03; $p = 0.8$). Multi-variate modelling did not reveal any factors that predicted a relative differential in subsequent outcomes.

Conclusion: EEN and systemic steroids are similarly efficacious therapies for new onset luminal CD in children. In Canada choice of therapy is influenced by CD location, but both therapies are frequently employed prior to IM or anti-TNF maintenance. Whilst initial EEN use is associated with less subsequent GCS exposure, initial use of EEN versus GCS did not appear to benefit longer term disease activity, treatment escalation, disease complication or linear growth.

Disclosure of Interest: Abbvie – AM Griffiths, A Otley, E Wine, HQ Huynh, JC deBruyn, K Jacobson, Sherlock M, Carroll MW, Church PC, Walters TD, El-Matary W; Janssen - AM Griffiths, A Otley, E Wine, HQ Huynh, JC deBruyn, K Jacobson, Carroll MW , Walters TD, El-Matary W; Merck – AM Griffiths, HQ Huynh, JC deBruyn, Jacobson K, Sherlock M, PC Church, TD Walters, El-Matary W.;Eli Lilly – AM Griffiths, Otley A; Pfizer -AM Griffiths; Gilead– AM Griffiths; Roche – AM Griffiths; Shire – AM Griffiths, A Otley; Takeda – A Otley.

P-053

Outcome of pediatric Crohn disease patients after steroid or exclusive enteral nutrition induction - preliminary data based on Hungarian Pediatric IBD Registry (HUPIR)

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Background: Exclusive enteral nutrition (EEN) is recommended as a first-line induction therapy for paediatric CD, instead of the corticosteroid (CS) therapy according to the guidelines. A few studies have shown that EEN provides early mucosal healing more often than CS, but the long-term benefits of EEN are just emerging. We retrospectively reviewed follow-up data of CD patients treated with EEN or CS as induction therapy, based on the Hungarian Paediatric IBD Registry (HUPIR).

Methods: HUPIR is a prospective nationwide database recording newly diagnosed paediatric IBD cases. Demographic details, localization, activity indices, and induction therapy are collected at diagnosis. The follow-up questionnaire includes information about relapse rate, surgical procedures, use of biologicals and extraintestinal manifestations. We evaluated the rate of relapses, bowel resections, need for biologicals in patients who received EEN or CS as induction after one and years of follow-up. We used the data of CD patients, who were registered between 1 January 2010 and 31 December 2015, and were followed-up for at least three years. Descriptive statistical methods and Chi Square test methods were applied.

Results: In the inclusion period, a total of 558 CD patients were registered, among them 113 (20%) started EEN and 263 (47%) patients received CS. At the three-year follow-up, we had data on 180 patients (180/367, 50%). At one-year children in the EEN group had similar rate of relapse (31% vs. 32%, $p=0.83$), of bowel resection (5% vs. 2%, $p=0.06$) and need for biologicals (21% vs. 25%, $p=0.35$) as the patients in the steroid group. Three years after diagnosis there was no significant difference in the rate of relapses (51% vs. 57%, $p=0.50$), of the need for biologicals (21% vs. 28%, $p=0.37$), of bowel resection (9% vs. 10%, $p=0.86$) in the frequency of extraintestinal manifestations occurring after diagnosis (11% vs. 12%, $p=0.28$). The rate of perianal disease appearing after the diagnosis was also similar ((11% vs. 12%, $p=0.28$)).

Conclusion: These findings suggest that outcome after EEN induction therapy is similar to outcome after the steroid treatment not only in short term, but also in mid-term follow-up based on our real-life population-based data.

The excess steroids use in paediatric inflammatory bowel disease in Poland: results from a multicentre audit using a web based steroid assessment tool

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Objectives and Study: Steroids are one of the most potent treatment options in acute flares for both Crohn's disease (CD) and ulcerative colitis (UC). Ineffectiveness in maintaining remission and significant side effects, including growth retardation limit their usefulness, especially in children. This is the first multicentre study analysing steroid use in paediatric inflammatory bowel disease (PIBD) in Poland, in both in-patients and out-patients settings.

Methods: We prospectively audited IBD patients in 17 paediatric IBD centres in Poland with the enrolment period of 6 months, ended on November 30th 2018. The online steroid assessment tool (SAT) and its supplementary paper form were applied to record steroid use in consecutive, unselected paediatric patients aged 2-18 years, with established diagnosis of IBD at least 3 months prior to the enrolment. Steroid dependence was defined according to the ESPGHAN's guideline as an inability to terminate steroids within 3 months without recurrent active disease or relapse requiring steroids within 3 months of stopping steroids.

Results: Of 1365 patients (50% CD, 46%UC, 4% IBD-U) 66% were in clinical remission. UC patients more common than CD, presented with moderate/sever disease (12.5% vs 7.7%, $p < 0.01$). 93% children were treated with 5-ASA, and CD patients were more frequent treated with thiopurines (75% vs 50%, $p < 0.001$) and anti-TNF (39% vs 14%, $p < 0.001$). In the previous 12 months, 35% IBD patients (44% UC, 28% CD; $p < 0.001$) had received steroids, that was more often used in an active disease (67% patients presented with moderate/severe disease). In multivariate analysis, disease activity was a predictor for the steroids exposure. The mean time duration of steroid use was 3.5 ± 2.1 mo and was longer in CD than in UC (3.8 ± 2.4 vs 3.3 ± 1.9 ; $p < 0.05$). Time of the longest steroid therapy was 13 mo., and 20% patients (21% UC, 12% CD) was exposed to more than one steroid course. 41% patients were unable to reduce steroids, while 14% had had a relapse within 3 mo. of stopping steroids that was no related to the type of disease. Of steroids exposed patients, 46% were classified as steroid dependent (47% CD, 45% UC). Moderate/sever disease activity increased risk for steroid dependency for UC (OR 2.88, CI 1.40-5.95), while CD patients previously treated with anti-TNF were more likely to experience steroid dependency.

Conclusions: We identified an inappropriate excess steroid use in 16% of Polish paediatric IBD patients. Excess steroid use differ between UC and CD, that may reflect the limited access for anti-TNF for PIBD patients in Poland. Routine steroid exposure asses should be considered as a quality of health care in PIBD.

Disclosure of Interest: The study was suported by the reaesrch grant from Abbvie

P-056

Comparing oral corticosteroid ≥ 30 mg/day use among pediatric and adult patients with newly diagnosed ulcerative colitis

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Objectives: Ulcerative Colitis (UC) has a relapsing-remitting disease course. Sparing use of oral corticosteroids (CS) ≥ 30 mg/day, as mono or combination therapy, are generally reserved for rapid relief of symptoms and induction of remission to achieve optimal therapeutic response. This analysis aimed to compare patient profiles of adult and pediatric patients newly diagnosed with UC who use ≥ 30 mg/day CS in a real world setting.

Methods: The Truven Marketscan commercial administrative claims database was used to explore the real-world utilization of ≥ 30 mg/day CS among pediatric (children 2- 11 years old and adolescents 12-17 years old) and adult (≥ 18 years old) UC patients. Patients were identified based on first diagnosis of UC during 1/Jan/2013 -31/Dec/2015 and were included in the analysis if they had an additional UC diagnosis during the 1-year post-index period. Patients with pre-specified, common inflammatory comorbid conditions associated with high doses of oral CS were excluded. The final sample was subsequently stratified based on number of days (d) [0, 1-7, 8-30, 31-90, 91-180, 181-365] on ≥ 30 mg/day oral CS during follow-up (1-year post diagnosis). Pre-index and post-index patient characteristics (demographics, medications, and health care resource use (HCRU)) are described.

Results: A total of 10,443 UC patients were included in this analysis consisting of 91 children (2-11 years old), 290 adolescents (12-17 years old), and 10,062 adults (18+ years old). Approximately, 40.66% of children and 46.90% of adolescents received corticosteroids during the 1-year post-index period, compared to only 14.62% of adults. In addition, 25.27% of children, 34.48% of adolescents, and 6.68% of adults received corticosteroids for more than 30 days during the 1-year post-index period. Among all subgroups, patients with ≥ 30 d of ≥ 30 mg/day CS use were more likely to be prescribed biologics. HCRU (including gastroenterologist visits, emergency room visits, and inpatient visits) was higher for patients receiving ≥ 30 mg/day of CS at least 1 day during the post-index period when compared to those not receiving ≥ 30 mg/day of CS. HCRU was higher among the pediatric subgroups (children and adolescents) when compared to adults (Table 1).

Conclusions: During a 1-year follow-up period, UC patients with a longer duration of ≥ 30 mg/day CS use were more likely to be on a biologic and had increased HCRU. This analysis of real-world data suggests that there is a subset of newly diagnosed pediatric and adult patients with UC who may require longer use of higher doses of oral CS to achieve optimal therapeutic response. This analysis also suggests that pediatric UC patients are more likely to be treated with corticosteroids and have higher HCRU when compared to the adult UC population.

	Children (2-11 years old)	Adolescents (12-17 years old)	Adults (18+ years old)
Total, N	91	290	10,062
UC/Crohn's Surgery During Post-Index; n (%)	4 (4.4%)	9 (3.1%)	280 (2.8%)
Gastroenterology Visit Post Index; n (%)	15 (16.5%)	100 (24.5%)	6,746 (67.0%)
ER Visit Post Index; n (%)	20 (22.0%)	71 (24.5%)	2,120 (21.1%)
Inpatient Visit Post Index; n (%)	36 (39.6%)	98 (33.8%)	1,026 (10.2%)
Outpatient Visit Post Index; n (%)	91 (100.0%)	290 (100.0%)	9,574 (95.2%)
Outpatient Visit Days During the Post-Index; mean (SD)	21.27 (26.42)	18.57 (22.17)	14.56 (24.03)

[Table 1. Healthcare Resource Utilization of Patients with Ulcerative Colitis]

P-057

Comparing oral corticosteroids ≥ 30 mg/day use among pediatric and adult patients with newly diagnosed Crohn's disease

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Objectives: Crohn's disease (CD) has a relapsing-remitting disease course. Sparing use of oral corticosteroids (CS) ≥ 30 mg/day, as mono or combination therapy, are generally reserved for rapid relief of symptoms and induction of remission to achieve optimal therapeutic response. This analysis aimed to compare patient profiles of adult and pediatric patients newly diagnosed with CD who use ≥ 30 mg/day CS in a real world setting.

Methods: The Truven Marketscan commercial administrative claims database was used to explore the real-world utilization of ≥ 30 mg/day CS among pediatric (children 2- 11 years old and adolescents 12-17 years old) and adult (≥ 18 years old) CD patients. Patients were identified based on first diagnosis of CD during 1/Jan/2013 -31/Dec/2015 and were included in the analysis if they had an additional CD diagnosis during the 1-year post-index period. Patients with pre-specified, common inflammatory comorbid conditions associated with high doses of oral CS were excluded. The final sample was subsequently stratified based on number of days (d) [0, 1-7, 8-30, 31-90, 91-180, 181-365] on ≥ 30 mg/day oral CS during follow-up (1-year post diagnosis). Pre-index and post-index patient characteristics (demographics, medications, and health care resource use (HCRU)) are described.

Results: A total of 8,909 CD patients were included in this analysis consisting of 215 children (2-11 years old), 487 adolescents (12-17 years old), and 8,207 adults (18+ years old). Approximately, 30.23% of children and 33.06% of adolescents received corticosteroids ≥ 30 mg/day during the post-index period, compared to only 13.59% of adults. In addition, 20.00% of children, 24.44% of adolescents, and 5.12% of adults received corticosteroids for more than 30 days during the 1-year post-index period. Among all subgroups, patients with ≥ 30 days of ≥ 30 mg/day CS use were more likely to be prescribed biologics. HCRU (including gastroenterologist visits, emergency room visits, and inpatient visits) was higher for patients receiving ≥ 30 mg/day of CS at least 1 day during the post-index period when compared to those not receiving ≥ 30 mg/day of CS. HCRU was higher among the pediatric subgroups (children and adolescents) when compared to adults (Table 1).

Conclusion: During a 1-year follow-up period, CD patients with a longer duration of ≥ 30 mg/day CS use were more likely to be on a biologic and had increased HCRU. This analysis of real-world data suggests that there is a subset of newly diagnosed pediatric and adult patients with CD who may require longer use of higher doses of oral CS to achieve optimal therapeutic response. This analysis also suggests that pediatric CD patients are more likely to be prescribed corticosteroids and have higher HCRU when compared to the adult CD population.

	Children (2-11 years old)	Adolescents (12-17 years old)	Adults (18+ years old)
Total, N	215	487	8,207
UC/Crohn's Surgery During Post-Index; n (%)	5 (2.3%)	34 (7.0%)	521 (6.3%)
Gastroenterology Visit Post Index; n (%)	49 (22.8%)	158 (32.4%)	5,382 (65.6%)
ER Visit Post Index; n (%)	51 (23.7%)	127 (26.1%)	2,221 (27.1%)
Inpatient Visit Post Index; n (%)	66 (30.7%)	163 (33.5%)	2,969 (36.2%)
Outpatient Visit Post Index; n (%)	215 (100.0%)	487 (100.0%)	8,188 (99.8%)
Outpatient Visit Days During the Post-Index; mean (SD)	29.47 (53.38)	21.57 (21.24)	21.25 (28.91)

[Table 1. Healthcare Resource Utilization of Patients with Crohn's Disease]

P-058

Steroid treatment for longer than two weeks leading to admission predicts higher colectomy rates in ulcerative colitis

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Objectives and Study: The value of second-line treatment and rescue therapy in acute severe colitis (ASC) has been established. There is lack of evidence to which factors determine adverse outcome in children with ulcerative colitis over time. Our aim was to identify risk factors for colectomy in children admitted for flare-up of ulcerative colitis.

Methods: We conducted a systematic retrospective case note review in our major tertiary GHN service and identified n=32 patients admitted for medical treatment of active ulcerative colitis. We divided patients into 2 cohorts: Group A (n = 10); received steroids >2 weeks before admission, and Group B (n = 22); received steroids < 2 weeks before admission or did not receive steroids prior to admission. We compared both groups regarding PUCAI scores, proportion of clinical remission, flare-up, colectomy, and co-medication (azathioprine/6-mercaptopurine, infliximab) after 1, 3 and 5 years of admission. Data were analysed using Fisher's exact test.

Results: The colectomy rate was significantly higher in Group A (received steroids >2 weeks) after 1, 3 and 5 years (Table 1). Patients in Group B were significantly higher on azathioprine treatment. Group B had a higher proportion of initial flare-up as acute severe colitis. Notably, both groups did not differ between median PUCAI score on all admissions, IV-steroid dosage (high or low dose protocol), infliximab treatment, or antibiotics given at first flare-up

Conclusions: Patients receiving steroids for longer than 2 weeks are at greater risk to requiring colectomy after 1, 3 and 5 years than patients admitted earlier. This effect was irrespective to the cumulative IV-steroid dosage, use of infliximab, or IV antibiotics, or initial flare-up as acute severe colitis. Azathioprine may provide protection against colectomy. Our study indicates the need to consider earlier escalation treatment for children not responding within two weeks of oral corticosteroids.

	Entire cohort (n = 32)	Group A (n = 10); received steroids >2 weeks before ASC admission	Group B (n = 22); received steroids <2 weeks before ASC admission or did not receive steroids	Fisher's test (P-values)
Flare up rate at 5 years, n (%)	13 (40.6%)	2 (20.0%)	11 (31.8%)	0.050*
Azathioprine/6MP rates at 1 year, n (%)	27 (84.4%)	7 (70.0%)	20 (90.9%)	0.293
Azathioprine/6MP rates at 5 year, n (%)	20 (62.5%)	3 (30.0%)	17 (77.3%)	0.018*
Infliximab rates at 1 year, n (%)	2 (6.3%)	1 (10.0%)	1 (4.5%)	0.534
Colectomy at 1 year, n (%)	3 (9.4%)	3 (30.0%)	0 (0%)	0.024*
Colectomy at 3 years, n (%)	4 (12.5%)	4 (40.0%)	0 (0%)	0.006*
Colectomy at 5 years, n (%)	5 (15.6%)	5 (50.0%)	0 (0%)	0.001*
Median PUCAI score	55 (43.8-65)	42.5 (40-56.3)	50 (45-55)	0.241
Antibiotics at first flare up, n (%)	17 (53.1%)	4 (40.0%)	13 (59.1%)	0.450

[Colectomy rates at 1 , 3 and 5 years]

Disclosure of Interest: SS has received speaker fee from MSD, Actavis, Abbvie, Dr Falk pharmaceuticals, Shire and received educational grant from MSD, Abbvie, Actavis and is an advisory board member for Abbvie, Dr Falk pharmaceuticals, Janssen and Vifor pharmaceuticals. MKHA has received speaker fees from Abbvie, and travel grants from Abbvie, Dr Falk pharmaceuticals, MSD/Janssen and Nutricia. CT has received speaker fees from Abbvie, Sanofi, Nestle and travel grants from Abbvie, MSD and Nutricia.

P-059

Thiopurines effectiveness in TDM-based clinical practice - a real life prospective cohort of pediatric IBD

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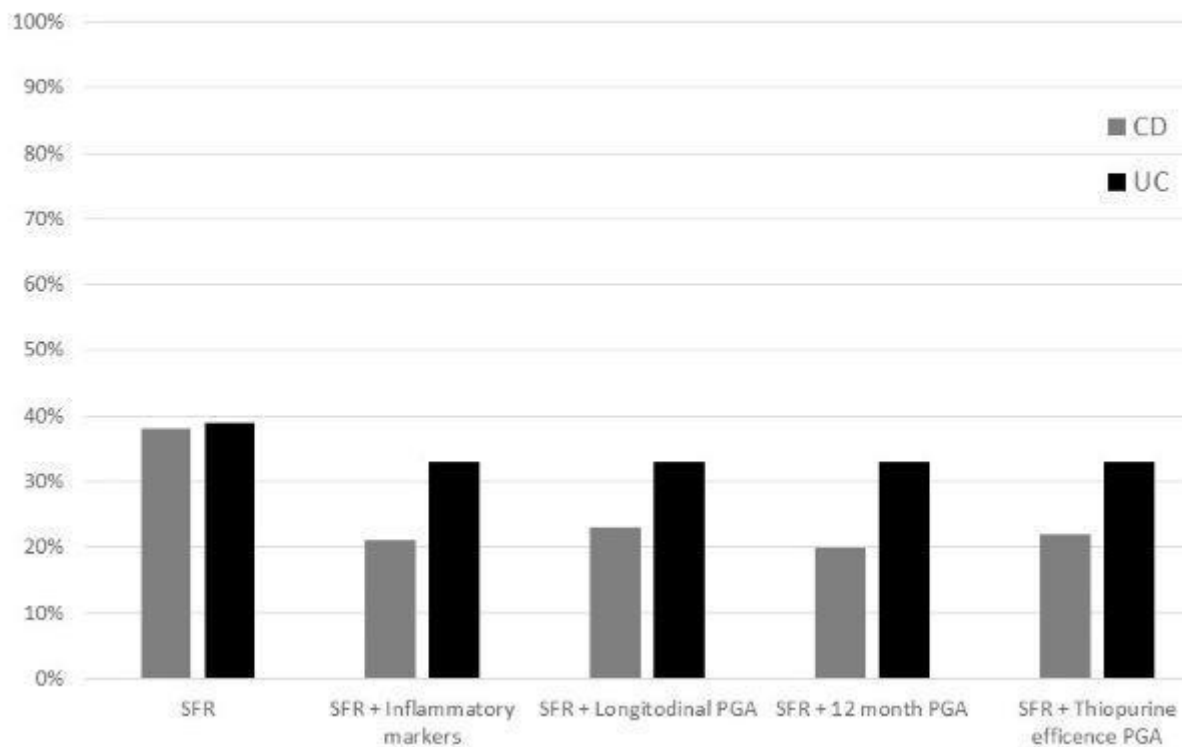
Objectives and Study: The use of thiopurines for IBD is declining due to data showing inferior effectiveness of thiopurines compared with biologics, together with concerns over toxicity. Nonetheless, in the era of personalized medicine, therapeutic-drug-monitoring (TDM)-based dosing may increase effectiveness and safety. This approach has not been evaluated in a prospective manner in children. We thus aimed to explore outcomes of thiopurine treatment and predictors of response in a prospective cohort of children with IBD treated with TDM-based dosing.

Methods: Children younger than 18 years with IBD treated with thiopurines were enrolled. Children starting thiopurines as combination therapy with biologics or for preventing post-operative recurrence were excluded. Explicit demographic and clinical data, laboratory results, and adverse events were recorded at baseline, 4 and 12 months, thereafter. Disease activity was measured using wPCDAI for CD and PUCAI for UC as well as physician global assessment (PGA). Dosing was guided and adjusted by TPMT activity measured at baseline and metabolites levels (6-TG and 6-MMP) at 4 months, as well as clinical response and toxicity. The primary outcome was steroid-free remission (SFR) without treatment escalation by 12 months, calculated based on the modified ITT principal. This study was approved by the local Ethical Committee.

Results: A total of 129 patients were included (74% CD and 26% UC/IBDU; mean age 12.3±3.7, and 59% males). TPMT mutation was noted in 119 (92%) (1 (1%) heterozygotes and 118 (99%) homozygotes). Change in the initial dose based on the metabolites levels at 4 months and clinical response was noted in 42% of all patients. Seventy-nine (82%) and 28 (85%) children completed at least 3 months of therapy without other treatments in the CD and UC groups, respectively, and 56 (58%) and 18 (55%) completed 12 months. Of the 107 patients who completed at least 3 months of therapy, 37 (47%) CD and 13 (46%) UC achieved the primary outcome of SFR (38% and 39% of the entire cohort), and 20 (21%) and 11 (33%) achieved the primary outcome with normal levels of ESR and CRP (Figure 1). At 4 months, MCV/WBC ratio and change in ANC values from baseline correlated with 6-TG levels ($r=0.33$, $p=0.02$ and $r=0.32$, $p=0.02$, respectively). Mild drug-related adverse events were recorded in 30 children (22%) the most common of which were . gastrointestinal symptoms ($n=11$, 9%), flu-like symptoms ($n=9$, 7%), and hepatotoxicity ($n=8$, 6%). None of the baseline variables predicted response in CD. In UC, SFR was associated with mean body weight (z-score 0.54 ± 1.5 in responders vs -1.1 ± 1.5 in non-responders; $p=0.01$) and median PUCAI score (12.5 (IQR 1.3-27.8) vs 45 (10-50); $p=0.02$). There were no cases of clinically-significant leukopenia, lymphoma or HLH.

Conclusion: In this real-life prospective cohort utilizing TDM-based dose optimization, thiopurines were safe and effective in both CD and UC. Normal CRP and ESR remission at 12 month was noted in 21% of CD children and 33% of UC children. Thiopurines remain a viable option in the treatment algorithm of paediatric IBD.

Figure 1



[*Typhorines outcome*]

Disclosure of Interest: Dan Turner received last 3 years consultation fee, research grant, royalties, or honorarium from Janssen, Pfizer, Hospital for Sick Children, Ferring, Abbvie, Takeda, Biogen, Neopharm, Uniliver, Atlantic Health, Shire, Celgene, Lilly, Roche

P-060

Thiopurine metabolites based dosing for azathioprine treatment in children with IBD

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Objectives and Study: Azathioprine is widely used for maintenance of remission in children with inflammatory bowel disease (IBD). Measuring thiopurine metabolites (6-TGN and 6-MMP) can aid optimising treatment and preventing toxicity. We report a proactive approach combining early metabolite measurements with IBD activity index to achieve optimal azathioprine dosing.

Methods: Retrospective reporting of thiopurine dosing, IBD activity indexes and thiopurine metabolites in 40 children with inflammatory bowel disease on azathioprine monotherapy. Additional treatments and azathioprine effect on blood counts were also examined, and children on combination biologic therapy excluded (5).

Results: 35 children (40% females) with IBD (24 Crohn's disease, 9 ulcerative colitis and 2 inflammatory bowel disease unclassified IBDU), mean age \pm SD (12.4 \pm 3.4). Mean effective azathioprine dose was 1.4mg/kg \pm 0.5, 6-TGN 280 \pm 151, 6-MMP 1022 \pm 1007. Disease activity index (Crohn's and UC paediatric specific) at the time of metabolite measurement 6.5 \pm 8. Twenty-three children did not require azathioprine dose adjustment, it was increased in 12.

Conclusions: Timely measurement of thiopurine metabolites and clinical assessment can provide a powerful tool to optimize azathioprine dosing and reduce serious adverse effects in children with IBD, and that a standard weight-based dosing may not be applicable.

P-061

Cost-effectiveness of the use of HLA-DQA1-HLA-DRB1 polymorphism to identify pediatric patients with inflammatory bowel disease at risk for azathioprine-induced acute pancreatitis

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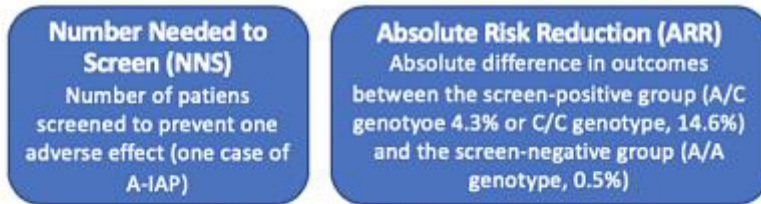
Objectives and Study: Thiopurines may be effective for maintaining remission in pediatric inflammatory bowel disease (IBD), but due to their low safety profile, the most recent evidence-based guidelines recommend they should be reserved as second-line therapy after 5-ASA has failed. One idiosyncratic adverse effect is acute pancreatitis and affects 2-7% of patients treated with azathioprine (AZA). Its development is unpredictable and usually leads to drug withdrawal. An association within the HLA-DQA1*02:01-HLA-DRB1*07:01 haplotype has been previously identified. The risk of pancreatitis during AZA-therapy was highly predictable and genotype-dependent: 0.5% for wild-type (A/A), 4.3% for heterozygous (A/C), and 14.6% for homozygous patients (C/C). The aim of our study was to conduct a cost-effectiveness analysis of the use of HLA-DQA1-HLA-DRB1 polymorphism to identify pediatric patients with inflammatory bowel disease at risk for azathioprine-induced acute pancreatitis (A-IAP).

Methods: Theoretical analysis of costs and benefits from routinely studying the HLA-DQA1*02:01-HLA-DRB1*07:01 haplotype in pediatric patients with IBD that are candidates for the use of azathioprine as maintenance therapy, in order to avoid using this treatment in those at risk of A-IAP. We calculated the number needed to screen (NNS), defined as the number of patients that need to be screened to prevent one adverse event, based on the available data. This was computed as the inverse of the Absolute Risk Reduction (ARR), defined as the difference in percentage outcomes between the related and un-related haplotype. The costs of the HLA typing were based on the INNO-LiPA® test (FUJIREBIO, Spain).

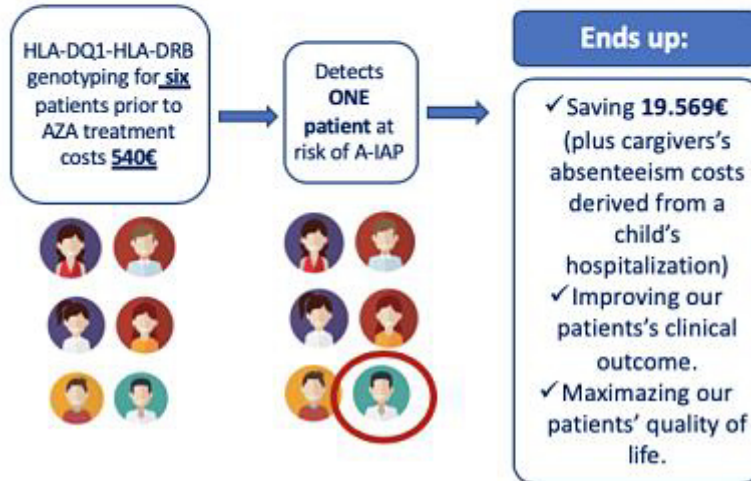
The costs of acute pancreatitis cases were based on the diagnosis-related group (DRG) weights applied by the Spanish Ministry of Health. These relative weights represent the expected cost of a particular kind of patient compared to the average cost of all the acute hospitalized patients.

Results: The cost of the screening for the haplotype was approximately 90€ per patient. Considering the previously reported incidence of A-IAP in the three possible genotypes; NNS was 5.4. NNS was rounded up to 6 patients, so the expected cost for avoiding one case of A-IAP was 540€. The A-IAP diagnose in the DRG 32nd version (DRG 282.3) has a mean weight of 1.15. The total cost of a case of A-IAP was about 20.109 € per patient. This leads to saving up to 19.569€ for every 6 patients screened before starting the AZA treatment.

Conclusion: Based on our results, routinely performing HLA-DQA1-HLA-DRB genotyping prior to initiation of AZA could be cost-effective in order to avoid A-IAP. Furthermore, the caregivers' absenteeism costs derived from a child hospitalization were not included in this analysis and would reinforce our conclusions. However, the costs derived from the therapeutic alternative that would be considered for those who could not receive AZA should be considered. But, most importantly, and beyond the economic rationale, preventing this potentially severe adverse effect could improve the clinical outcomes of our patients and allow an individualized management. This patient-tailored approach should be the goal of clinicians, not only to optimize the use of Public Health Funds, but also to maximize our patients' quality of life.



NNS = 1/ARR
NNS = 1/(0.19-0.005) = 5.4



[Figure 1: NNS calculation and results interpretation.]

P-062

Differentiation of patient-specific induced pluripotent stem cells in pancreatic exocrine cells to model thiopurine induced pancreatitis in pediatric patients with Crohn's disease

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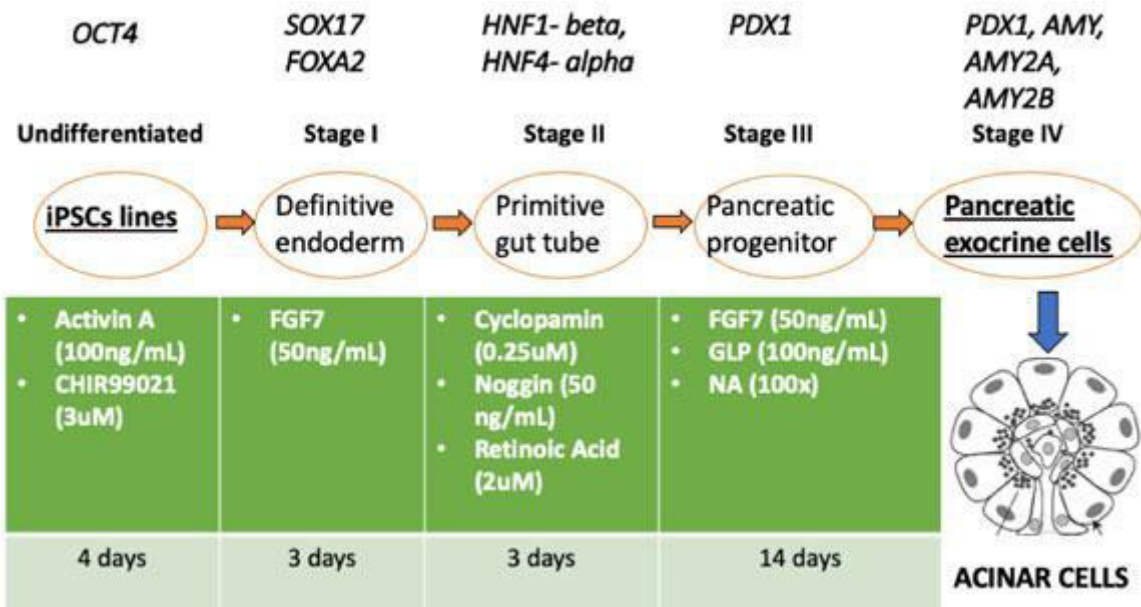
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Objectives and Study: Patient induced pluripotent stem cells (iPS) can be used to model diseases and predict drug adverse effects in a personalized way. Thiopurines are used to treat Crohn's disease (CD), however, about 5% of patients develop pancreatitis, a severe idiosyncratic reaction characterized clinically by abdominal pain and high pancreatic enzymes in blood and urine. The mechanism of thiopurine induced pancreatitis (TIP) is unknown and no biomarker is available for clinicians to prevent it. TIP can be modelled by differentiating CD-iPS to exocrine pancreatic cells, to discover biomarkers useful for its prevention. The experimental conditions for CD-iPS differentiation and for the evaluation of the *in vitro* sensitivity to thiopurines were assessed.

Methods: iPS were obtained by reprogramming peripheral blood mononuclear cells of 6 CD patients that developed (n=3) or not (n=3) TIP using viral transduction. iPS were differentiated in pancreatic exocrine cells using a 4 steps protocol (Figure 1) (1). Differentiation efficiency was confirmed by PCR real time quantifying the pluripotency marker *OCT4*, the definitive endoderm (DE) marker *SOX17*, the pancreatic progenitor marker *PDX1* and the pancreatic exocrine marker amylase. *PDX1* and amylase were quantified also by immunochemistry. Amylase level was compared to that of the human pancreatic duct epithelial line H6C7. CD-iPS of one patient with and one patient without TIP were treated with azathioprine (AZA), mercaptopurine (MP), thioguanine (TG) for 72 h and cytotoxicity was analyzed by MTT. Also H6C7 was treated with MP and TG for 72 h. Cell cycle of CD-iPS was analyzed by propidium iodide assay and compared to that of H6C7 line.

Results: iPS presented the highest expression of *OCT4* while differentiated cells the lowest. *SOX17*, as expected, was higher in DE with respect to iPS. Amylase and *PDX1* were the highest in the exocrine cells. Amylase level of exocrine cells was higher with respect to the duct H6C7 line. Interestingly, MTT assay showed a higher sensitivity of the TIP-iPS (AZA $-\log EC_{50}$ 5.84±0.06 M; MP 6.86±0.05 M; TG 6.88±0.05 M) with respect to the not TIP-iPS (AZA $-\log EC_{50}$ 5.58±0.07 M; MP 6.08±0.09 M; TG 6.41±0.05 M) (p-value, t test: MP and TG < 0.0001; AZA < 0.001). H6C7 line was slightly sensitive to TG ($-\log EC_{50}$ 3.17±0.07 M) while resistant to MP (EC_{50} >1.0×10⁻³M). Preliminary analysis on cell cycle showed a higher proliferation of CD-iPS (no TIP-iPS: G0 37.6%, S 24.0%, G2/M 38.4%; TIP-iPS G0 25.0%, S 36.0%, G2/M 39.0%) with respect to the H6C7 (G0 64.2%, S 19.7%, G2/M 16.1%) line.

Conclusion: Analysis of differentiation markers confirmed the pancreatic differentiation of CD-iPS. The higher expression of amylase of exocrine cells with respect to the H6C7 duct line suggests the acinar development. Interestingly, thiopurine treatment resulted more cytotoxic for TIP-iPS than not TIP-iPS, however this result has to be confirmed in the remaining 4 patients. Thiopurine cytotoxic effect is strictly correlated to proliferation due to the cell cycle-specific mechanism of these drugs interfering with the new DNA strand formation. The faster proliferation of both CD-iPS can explain their higher sensitivity with respect to H6C7. Analysis is ongoing to confirm results obtained and to analyze sensitivity of differentiated cells



[Fig. 1]

P-063

Clinical experience of pre-treatment pharmacogenetic test of TPMT and NUDT15 gene in Korean pediatric patients with Crohn's disease

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Introduction: *TPMT* gene variant are known as important gene associated with thiopurine metabolism. And *NUDT15* gene variant was also noticed as a key genetic variant which associated with early leukopenia and alopecia associated with thiopurine usage. Our previous study demonstrated 9.9% of azathioprine(AZA) induced early leukopenia in Crohn's disease(CD) patients and found relatively high incidence of *NUDT15* c.145C>T variant present rather than *TPMT* gene variant in Korean pediatric CD patients. Though, since 2016, we conducted *TPMT* and *NUDT15* gene studies at the time of CD diagnosis. This study is a follow-up study of our previous study on whether there was a change in the clinical treatment policy corresponding to the pre-treatment pharmacogenetic (PG) test.

Methods: Between 2016 and April 2019, newly diagnosed pediatric CD patients in Pusan National University Children's Hospital were recruited. Electronic medical records were analyzed retrospectively. PG test results were analyzed. Initial AZA prescription doses and maximal doses were collected according to the PG test results. Adverse event of AZA was investigated.

Results: 61 patients underwent PG study at the time of CD diagnosis. Nine patients (14.8%) revealed *NUDT15* c.145C>T heterozygote variants and one patient (1.6%) revealed *TPMT* heterozygote variant. 43 patients (70.5%) were prescribed AZA. Among nine patients with *NUDT15* c.145C>T heterozygote variant, only four patients (44.4%) prescribed AZA as maximal dose of 1.14 ± 0.26 mg/kg/day. One patient with *TPMT* heterozygote variant used AZA of 1.46 mg/kg/day. 38 patients started AZA as 1.07 ± 0.52 mg/kg/day and increased dose up to 2.20 ± 0.82 mg/kg/day. None of them experienced leukopenia or alopecia due to AZA. There were no cases discontinued AZA due to drug adverse event.

Conclusion: When genetic variants were found, there was a tendency to treat with drugs other than AZA. PG tests prior to use of azathioprine changes could dramatically prevent adverse event associated with AZA usage.

P-064

Characteristics of biological therapy in paediatric patients with Crohn's disease based on data of a nation-wide incident cohort of HUPIR

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Introduction: Pediatric Crohn's disease (CD) is a chronic inflammatory disorder of the gastrointestinal tract. Curative therapy is currently not available, however, biological therapy (BT) can induce mucosal healing and improve life quality. Therefore, establishing the target population, who benefit from BT without long-term side-effects would be essential. However, the indication is different in different countries mainly due to financial reasons. Our aim was to evaluate the therapeutic practice regarding the BT in pediatric CD in Hungary, based on the data Hungarian Pediatric IBD Registry (HUPIR).

Methods: HUPIR is a nation-wide, prospective registry of newly diagnosed paediatric patients with Inflammatory bowel disease (IBD) (0-18 years) since 1st of January 2007. Patients are followed-up yearly: basic data, disease activity, number of relapses, therapy (medication and surgery), and extraintestinal manifestations are registered. We have analyzed data of patients diagnosed between 2010-2017, and compared the rate of (BT) and relapses applied after years and three years of diagnosis. Descriptive statistical methods for data analysis and Kaplan-Meier analyses for the rates of relapses, bowel resection and biological therapy during the follow-up were applied.

Results: Between 2010-2017, 801 paediatric CD patients were registered. From the diagnosis, 20% of patients received BT within the first year, 17% in the second year, 15% in the third year, 16% in the fourth year and 20% in the fifth year. Relapse rates were 27%, 17%, 19%, 16% and 17% within these intervals, respectively. The rate of administration of BT within the first year after the diagnosis did not change between 2010-2017 (12-18%), similarly to the rate of BT within three years of diagnosis (15-20%).

Conclusion: Between 2010-2017 we did not find any time trend in the use of BT. Meanwhile in other countries there was a definite increase as the „treat to target” strategy has become widespread. Our lower results probably reflect the different regulation rules of BT in Hungary hence after one year of successful BT the drug must be stopped.

P-065

Trends of utilization of tumor necrosis factor antagonists in children with inflammatory bowel disease: a canadian population-based study

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Objectives and Study: Anti-tumor necrosis factor (TNF) agents have revolutionized treatment of inflammatory bowel disease (IBD). Population-based studies describing the prevalence of anti-TNF utilization in children with IBD are scarce. We aimed to describe the trend of utilization of anti-TNF agents in children with IBD over time.

Methods: We performed survival analyses for all persons diagnosed with IBD prior to age 18y and identified in The University of Manitoba IBD Epidemiology Database to determine the time from diagnosis to first anti-TNF in different eras (2005-2008, 2008-2012, 2012-2016).

Results: There were 291 persons diagnosed with IBD [157 Crohn's disease (CD), 134 ulcerative colitis (UC)] prior to age 18y. The likelihood of being initiated on anti-TNFs by 1, 2 and 5 years post-diagnosis was 18.4%, 30.5% and 42.6% respectively. The proportion of persons under < 18y using anti-TNFs increased over time; in 2010, 13.0% of Crohn's disease (CD) and 4.9% of ulcerative colitis (UC); by 2016 60.0% of CD and 25.5% of UC were actively using an anti-TNF agent. For those diagnosed after 2012, 42.5% of CD and 28.4% of UC had been started on an anti-TNF agent within 1 year of IBD diagnosis. There was an increase over time in the likelihood of initiating anti-TNF therapy without prior IM exposure (prior to 2008: 0%, 2008-2012: 18.2%, 2012-2016: 42.8%, $P < 0.001$). The median cumulative dose of corticosteroids in the year prior to anti-TNF initiation significantly decreased over time (2005-2008: 4360mg; 2008-2012: 2010mg, 2012-2016: 1395mg prednisone equivalents, $P < 0.001$).

Conclusions: Utilization of anti-TNF agents has been increasing over time, and more recently they are being used earlier in the course of pediatric IBD. It was reassuring to document the decline of cumulative corticosteroid use in the recent years especially in children with CD, suggesting that one trade off to the increased costs of increasing anti-TNF use will be reduced ill effects from corticosteroids. More studies on long term costs associated with increased utilization of anti-TNF agents in children with IBD are warranted

Disclosure of Interest: This work was supported by Crohn's and Colitis Canada Grants in Aid of Research. Dr El-Matary served as an advisory board member for Janssen, Canada and Abbvie Canada

P-066 (Poster of Distinction)

Trends in TNF-alpha inhibitor utilization in children with IBD during the last 10 years: 2009-2018

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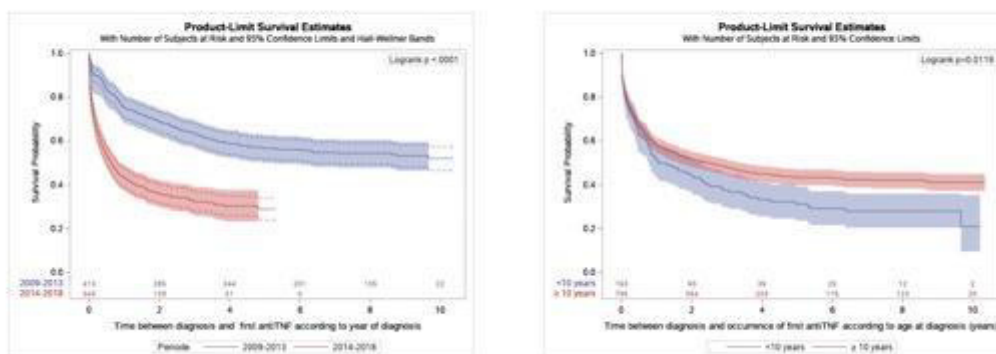
Objectives and Study: Since the last decade, anti-TNF have been increasingly used in the treatment of inflammatory bowel diseases (IBD), but the pattern of use is still not completely defined, especially in the pediatric population. We aimed to define the pattern of use of these monoclonal antibodies and the associated factors during the past ten years.

Methods: We conducted cross-sectional analysis of consecutive children with IBD (Crohn's disease (CD), ulcerative colitis (UC) or unclassified colitis (IBDU)) at CHU Sainte-Justine who had received a treatment with an anti-TNF (Infliximab (IFX) or Adalimumab (ADA)) between January 2009 and October 2018. The primary outcome was the time between IBD diagnosis and the initiation of TNF-alpha inhibitor over the years. The secondary outcomes defined as the proportion of patients receiving that treatment within three months of diagnosis (early treatment), and the factors associated with early initiation (< 3 months after IBD diagnosis) were analysed using survival analysis and Kaplan-Meier curves.

Results: Among the 962 patients diagnosed between January 2009 and December 2018, [(median (IQR) age at diagnosis 13.9 (4.5) years; 49.1% female; CD (n=651), UC (n=180), IBDU (n=131)], a total of 547 (56.8%) were exposed to anti-TNF. The median (IQR) PCDAI at diagnosis was 32.5 (20.0) for CD, and the median (IQR) PUCAI was 50.0 (35.0) in UC/IBDU. The median (IQR) age at start of anti-TNF was 14.1(4.5) years. The first exposition to anti-TNF was IFX (90%), or ADA (10%). Overall, the median (IQR) interval between IBD diagnosis and the initiation of TNF-alpha inhibitor was 117 (346) days. The median (IQR) interval was 354.0 (940.0) days for patients diagnosed in 2009-2010 and declined to reach 26.0 (101.0) days in 2017-2018. The rate of early treatment (< 90 days) was 4,8% in 2009 and gradually increased to reach a maximum of 42.9% in 2018 (Table 1). In the cohort as a whole, the proportion of early treatment with anti-TNF was higher for CD (27.9%) and UC (31.0) than IBDU (6.9%), $P < 0.0001$. A younger age at diagnosis was associated with an earlier start of anti-TNF (Hazard ratio = 1.40 (95% CI = 1.13-1.74); $P = 0.0024$). (Figure1)

Conclusion: More than 50% of children are exposed to anti-TNF after a median follow-up of 4,1 years. Over the last few years, anti-TNF, are being used earlier in the course of IBD in children. A long-term follow-up of this cohort would be useful to assess whether the early anti-TNF approach impacts the long-term durability of remission and the long-term probability to remain under these drugs.

Figure 1. Association between first anti-TNF alpha and : (1) Year of diagnosis and (2) Age at diagnosis



[Figure 1. Association between first anti-TNF alpha and: (1)Year of diagnosis and (2)Age at diagnosis]

P-067

Standard IFX dosing is ineffective in the majority of PIBD patients, with baseline albumin identified and replicated as a key determinant of post induction IFX level in two diverse PIBD cohorts

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Objectives: To evaluate the effectiveness of infliximab (IFX) induction regimes in attaining therapeutic post induction levels in 2 paediatric inflammatory bowel disease (PIBD) cohorts; to investigate baseline laboratory values and patient factors as predictors of post-induction levels.

Methods: 62 patients from Glasgow, Scotland (Cohort 1 (C1) - biosimilar IFX; standard induction of 5mg/kg at 0, 2 and 6 weeks with 8 weekly maintenance thereafter) and 78 patients from Vancouver, Canada (Cohort 2 (C2) [replication cohort] - originator IFX; variable dose induction regime) were included in the study. Baseline characteristics and laboratory values from time of IFX initiation were recorded. A Mann-Whitney U Test was used to analyse the relationship between IFX trough levels and lab parameters.

Results:

n(%)	COHORT 1 (n=62)	COHORT 2 (n=78)
CROHN'S DISEASE	50 (81%)	57 (73%)
MALE	34 (55%)	42 (54%)
INDICATION - ACTIVE LUMINAL DISEASE	45 (73%)	52 (67%)
BASELINE PGA MILD/MODERATE	42 (68%)	52 (67%)
HYDROCORTISONE COVER	59/60 (98%)	28 (36%)
CO-IMMUNOSUPPRESSION AT INITIATION	59 (95%)	33 (42%)
STEROIDS AT INITIATION	22 (36%)	21 (27%)

[Table 1: Cohort demographics, indication for infliximab and co-prescribed medications]

The median dose 4 troughs in C1 & C2 were 1.85 (IQR 3.38) and 4.25 (IQR 7.8) respectively. 18/62(29%) C1 patients and 10/78(13%) C2 patients had a pre dose 4 IFX trough of < 0.8mg/L; 39/62(63%) C1 patients and 32/78(41%) C2 patients had a trough of < 3mg/L; and 51/62(82%) C1 patients and 44/78(56%) C2 patients had a level < 5mg/L. In C2 patients who had a trough level < 3mg/L pre-dose 4, 62% (20/32) had dose adjustment documented prior to this. The IFX of 40/62(65%) C1 patients and 39/78(50%) C2 patients were escalated following the dose 4 level. Baseline median albumin was lower than and replicated within cohorts in those with pre-dose 4 IFX levels of:

- < 0.8mg/L: C1 (34.5g/L vs 37g/L in IFX ≥0.8mg/L, p=0.02); C2 (30g/L vs 37.5g/L in IFX ≥0.8mg/L, p=0.002)
- < 3mg/L: C1 (35g/L vs 37g/L in IFX ≥3mg/L, p=0.04); however this did not reach significance in C2 (34.5g/L vs 38g/L in IFX ≥3mg/L, p= 0.05)
- < 5mg/L: not significant in C1 (35g/L vs 37g/L in IFX ≥5mg/L, p=0.45); however this was significant in C2 (35g/L vs 39g/L in IFX ≥5mg/L, p=0.006)

Additional data within C2 showed median IFX level pre-dose 3 was 9.6mg/L (IQR 8.3). Baseline albumin was lower in those with low IFX levels pre-dose 3 (32g/L in IFX < 3mg/L vs 38g/L in IFX

≥3mg/L, p= 0.009 and 32g/L in IFX < 5mg/L vs 38g/L in IFX ≥5mg/L, p=0.002).

In the combined cohort (C1+2), patients with a baseline albumin ≤30g/L had significantly lower IFX levels pre dose 4 (1.4mg/L vs 3.55mg/L in those with albumin >30g/L (p=0.0003)). In patients with an albumin ≤30g/L, 6/26 (23%) achieved a dose 4 trough level of ≥3mg/L; however 5/6 (83%) of these patients received a non-standard (higher dose or reduced dose interval) induction regime, meaning only 1/26 (4%) of patients had a trough ≥3mg/L on standard treatment.

Conclusions: Standard IFX induction regime is ineffective at achieving relevant post-induction levels (>5mg/L) in the majority of patients regardless of IFX type. We suggest that adjustment of initial IFX prescribing based on baseline albumin (e.g. a higher dose given to patients with albumin < 30) and subsequent IFX levels will improve post-induction IFX levels and consequently clinical outcomes for a greater majority of patients.

Disclosure of Interest: VG:speaker's/conference fees - Ferring, Abbvie LC:conference fees - Ferring, Tillots LG:research consultancy session - Lilly RHansen: speaker's fees/travel support/medical board meetings - MSD Immunology, Dr Falk, Nutricia, 4DPharma KJ:Abbvie speakers bureau; Jansen adboard SL:Abbvie speakers bureau; Jansen adboard RKR speaker's fees/travel support/medical board meetings - Nestle, MSD Immunology, AbbVie, Dr Falk, Takeda, Napp, Mead Johnson, Nutricia, 4DPharma Remaining authors: nil declared

P-068 (Poster of Distinction)

Infliximab in young pediatric IBD patients: it is all about the dosing - a multicenter study from the pediatric IBD Porto group of ESPGHAN

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Objectives and Study: Infliximab (IFX) is frequently used in (paediatric) inflammatory bowel disease (IBD) patients refractory to corticosteroids and- or immunomodulators. IFX is administered intravenously using weight-based dose (5 mg/kg) for all IBD patients during the induction (infusion at weeks 0, 2 and 6) and maintenance phase (every 8 weeks). However, response rates to IFX differ significantly within the (paediatric) IBD population. We aimed to assess IFX pharmacokinetics (PK), based on existing therapeutic drug monitoring (TDM) data in a population of paediatric inflammatory bowel disease (PIBD) patients < 10 year (yr) and to compare these to PIBD patients >10 yr.

Methods: TDM data were collected retrospectively in 15 European and Canadian centres. Children treated with IFX between 2004-2016 were included, in case IFX was started as IBD treatment < 10 yr and PK data were available. Patients were excluded in case of diagnosis of monogenetic disease. These data were compared to a control group of PIBD patients >10 yr with PK data of IFX treated PIBD patients in a large tertiary hospital.

Results: One-hundred and ten young PIBD patients (YP) (< 10 yr) and 50 older PIBD patients (OP) (>10 yr) were eligible for the study. Median age at initiation of IFX treatment was 8.3 years [IQR 6.9-8.9] in the YP, and 14.3 [IQR 12.6-15.6] in the OP group. IFX trough levels (TLs) and dosing were not significantly different between ulcerative colitis and Crohn's disease patients (p=0.281), thus data have been pooled. The median interval between IFX infusions was significantly shorter (median interval days 49[IQR 39-56] vs. 56[IQR 55-56]; p< .001), while the dose (median dose 8 [IQR 5-10] mg/kg vs. 5[IQR 5-8,5] mg/kg; p=0.013) was significantly higher in the YP than OP at one yr of scheduled IFX maintenance treatment. Data of YP were comparable to those of very YP(< 6 yr) (n=7; median interval days 42[IQR 42-56](P=0.992); median dose 5[IQR 5-10]mg/kg (p=0.447)). In 72% of YP TLs were below the recommended range (>5.4 ug/ml) at 14 weeks. Multivariate analysis showed an association between lower IFX-TLs and antibodies to infliximab (ATI)positivity (odds ratio (OR) 1.384; 95%CI 0.919-1.849; p< 0.001), a lower dose (hazard ratio (HR) 0.1; 95%CI 0.011-0.188; p=0.027) and a longer interval in days (HR 0.02; 95%CI 0.028-0.010; p< 0.001). Nonetheless, this association wasn't found for use of combination therapy (OR -0.32;-0.905-0.263; p=0.28). Significantly more YP developed ATI during follow up compared to the OP group (41% in YP (median 798 days) vs. 26% in OP (median 1334 days), p=0.004). Despite increased immunogenicity, this did not lead to a statistically significant higher rate of loss of response (31% in YP and 48% in OP, p=0.58). There was no significant difference in duration of response to IFX between both age groups (after 2 years 53% (n=29) in YP vs. 63% (n=26) in OP; p=0.24).

Conclusion: We advise intensification of the IFX induction scheme in PIBD patients < 10 yr. Since several other patient factors influence trough levels, active TDM is required to evaluate and personalize treatment strategy. Nonetheless, development of a PK model and prospective trials are crucial to confirm our findings and further determine an ultimate treatment regimen for YP IBD patients.

P-069

Therapeutic Infliximab levels and sustained clinical remission can be achieved with lower Azathioprine doses in patients on dual therapy.

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Objectives: A combination of immunomodulators and biologic agents were proposed as efficacious in the treatment of paediatric inflammatory bowel disease (pIBD). Reduced antibody formation and improved clinical outcomes outweigh possible adverse events arising from combined treatment. Drug metabolite and infliximab antibody (IFA) monitoring have become common practice, supported by current international guidelines for pIBD management. There is however a paucity of data on optimal drug/metabolite levels in children receiving dual therapy. We aim to establish optimal azathioprine (AZA) dosing and thiopurine (TP) metabolite levels in combination therapy with infliximab (IF) to achieve clinical response and maintain remission.

Methods: We retrospectively reviewed 19 IBD patients with a median follow up of 17 months (IQR: 9-21). All subjects were commenced on AZA and stepped up to combination therapy with IF. Crohn disease (CD) patients received concomitant exclusive enteral nutrition and ulcerative colitis (UC) patients had at least one course of steroids and were maintained on aminosalicylates throughout. Disease activity indices (PCDAI, PUCAI) were determined at each outpatient clinic assessment. TP methyltransferase (TPMT) activity, AZA dose, thioguanine nucleotide concentration (6thioguanin, 6TGN; 6methylmercaptapurine, 6MeMP), IF through level (IFL), IFA and biochemical markers were measured at certain time intervals (To: IF initiation; T1, 2, 3: time elapsed in months from To). 6TGN and 6MeMP were included if values were collected up to two months prior to IFL.

Results: 19 patients (63% male) were identified (CD:13, UC:4, IBDU:2) with median age at diagnosis of 13.6 years (IQR:9.4-14.4). Disease distribution for CD patients was ileocolonic (53.4%), isolated small bowel disease (23.1%), and fistulising disease (30.8%) whereas 80% of UC had pancolitis. 17 patients had normal TPMT activity and two subjects were within carrier range (both 22pmol/h/mgHb). Patients started on IF at a median period of 9.0±8.3months from time of diagnosis. The majority had moderate to severe disease (78.9%) with therapeutic 6TGN:336±104.8 and 6MeMP:802±645.4. Mean AZA dose before initiation of IF was 1.4mg/kg/day. Serial metabolite concentrations, IFL and IFA were collected at T1:4.2±2.2, T2:12± 5.1 and T3:22±6.1 months. Children on combination therapy gradually reduced the AZA dose over a period of two years from 1.2 to 1.0mg/kg/day with a subsequent decrease of 6TGN and 6MeMP (272 to 178 and 622 to 290 respectively). 89.5% of patients had completed a standard IF induction course followed by 5mg/kg every 8 weeks. The first IFL was 4.76±4.4 and subsequently 3.11±1.54 (T2) and 4.82±2.92 (T3). IFL remained unchanged despite treatment frequency and dose escalation. Two patients developed IFA within the first 5 months from initiating IF with therapeutic 6TGN throughout the observed period. None of our patients experienced any adverse events. 68.3% of patients remained in remission one year after initiating combination therapy.

Conclusion: This retrospective study demonstrates that actively reducing AZA doses when used in combination with IF results in stable IFL. Our data suggests that lower than previously reported AZA doses and 6TGN levels are sufficient in preventing IFA formation and achieving clinical remission.

P-070

Experience with therapeutic drug monitoring (TDM) on Infliximab (IFX) in paediatric inflammatory bowel disease (pIBD)

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Objectives and Study: IFX is effective in treatment of pIBD. Low IFX trough levels and high antibodies to IFX (ATI) are associated with loss of response to IFX. Optimizing therapy with early trough levels and maintenance of monitoring has been suggested to be effective in the pIBD management. We aimed to evaluate whether proactive TDM with ATI is enabling clinicians to improve clinical outcomes, additionally to looking at biomarkers and PCDAI/PUCAI indices. Data suggest that drug levels between 5-10 mg/l with negative ATI should be aimed to improve clinical outcomes and biomarkers.

Methods: Retrospective review over 5 years of pIBD patients (n= 55) treated with IFX (5 mg/kg, 8 weekly); Crohn's disease [CD]=34; Ulcerative Colitis [UC]= 10; Inflammatory Bowel Disease Unclassified [IBDU] = 6; Early Onset Inflammatory Bowel Disease [EOIBD]=4; Males= 29, age at diagnosis 3-14 years, median 9. All patients were additionally on Azathioprine. 3 groups were identified: group 1 included patients with IFX level pre 4th dose < 0.8 mg/l; group 2 were patients with IFX levels between 0.8- 5 mg/l and group 3 patients with IFX levels > 5 mg/l

Results: IFX and ATI levels pre 4th dose were available for 34 patients, with IFX median level=2.50 mg/l (range 0.8 -31.6) and ATI median=0mg/l (range 0-203).

Group 1: n=5(14.7%). In 4/5 (80%) patients treatment were escalated to 10 mg/kg. 50% had negative ATI pre 4th dose, but developed ATI afterwards, 50% already had ATI before escalation of treatment. 3/4 patients went in to clinical remission. One was switched to Adalimumab (ADA).

Group 2: n= 16 (47%). IFX median levels=2.2mg/l (range 0.9-4.7), ATI median level=0 (range 0-203). 3/15 (20%) were switched to ADA: 1 for allergic reaction to IFX, the remaining 2 did not clinically respond. 5/15(33%) patients continued on IFX 5 mg/kg 8 weekly with clinical response. In 7/15(47%) of patients treatment was escalated by either double dosing or shortening intervals. Only 3/15(20%) developed ATI. The PUCAI/PCDAI decreased from mild to quiescent in 11/13, in 2/13 patients worsening of symptoms occurred leading to escalation of treatment.

Group 3: n=13(38%). IFX median level=10mg/l(range7.8 -27), ATI median level=0 (range 0-54). 10/13 (77%) patients remained on 5 mg/kg 8 weekly; 2 patients switched to ADA (1 for allergic reaction to IFX); in 1 patient the IFX interval was shortened to 6 weekly, going into clinic remission. The PUCAI/PCDAI decreased from moderate to inactive in 8/10 (80%), 2/10 (20%) patient had quiescent disease.

Conclusions: Our study suggests that proactive TDM approach improved clinical outcomes (PCDAI/PUCAI) in all 3 groups by increasing and maintaining adequate drug levels and reduction ATI in some patients.

P-071 (Poster of Distinction)

Infliximab trough levels are not associated with transmural healing at 1 year treatment in paediatric Crohn's disease patients

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Objectives and Study: Recent data in literature have demonstrated the association between infliximab (IFX) trough levels and mucosal healing (MH) in Crohn's disease (CD). We aimed to investigate whether IFX trough levels were associated with TH in paediatric patients with CD at 1 year treatment with IFX.

Methods: Paediatric patients with CD in whom IFX trough level tests, magnetic resonance enterography (MRE), and colonoscopies had been conducted simultaneously at 1 year treatment with IFX were included in this multicentre retrospective cross-sectional study. TH was defined as wall thickness ≤ 3 mm with the absence of ulcers, oedema, contrast enhancement, and complications on all ileocolonic segments evaluated by MRE. MH was defined as a Simple Endoscopic Score for Crohn's disease (SES-CD) < 3 on colonoscopy. Interval shortening between infusions to 4-6 weeks had been done when loss of response was suspected based on clinical symptoms. The association between IFX trough levels and TH, as well as IFX trough levels and MH were investigated.

Results: A total 56 patients were included in this study. MH and TH were observed in 60.7% (34/56) and 23.2% (13/56) of patients, respectively. IFX trough levels were significantly higher in patients with MH compared to those without MH (median 5.6 $\mu\text{g/mL}$ vs. 3.4 $\mu\text{g/mL}$, $P = 0.002$), while IFX trough levels were not statistically significant between those with and without TH (median 5.4 $\mu\text{g/mL}$ vs. 4.7 $\mu\text{g/mL}$, $P = 0.574$). The interval between IFX infusions had been shortened in 21.4% (12/56), and IFX trough levels were significantly higher in those whose intervals had been shortened (7.8 ± 4.3 $\mu\text{g/mL}$ vs. 4.7 ± 1.9 $\mu\text{g/mL}$, $P = 0.029$). No significant difference was observed in rates of MH between patients whose intervals were shortened or not (58.3% vs. 61.4%, $P = 1.000$). Although a statistical significance was not observed, the proportion of patients with TH was relatively lower in those whose intervals were shortened compared to those receiving IFX by standard intervals of 8 weeks (0% vs. 29.5%, $P = 0.078$). According to univariate logistic regression analysis, serum albumin and SES-CD at 1 year treatment with IFX were significantly associated with transmural healing (OR = 10.16, 95% CI = 1.37-92.62, $P = 0.028$, and OR = 0.60, 95% CI = 0.32-0.89, $P = 0.046$, respectively). However, these associations were not significant according to multivariate analysis (OR = 7.15, 95% CI = 0.82-79.32, $P = 0.086$, and OR = 0.60, 95% CI = 0.32-0.91, $P = 0.060$, respectively). Meanwhile according to multivariate logistic regression analysis, IFX trough levels and disease duration to IFX initiation were associated with MH (OR = 1.82, 95% CI = 1.27-2.62, $P = 0.001$, and OR = 0.43, 95% CI = 0.21-0.87, $P = 0.02$, respectively).

Conclusion: Trough levels of IFX were associated with MH but not with TH at 1 year treatment with IFX in paediatric CD patients treated according to infusion intervals based on clinical symptoms. Further studies regarding long-term TH outcomes and proactive dosing based on therapeutic drug monitoring may better clarify whether an association between IFX trough levels and TH exists or not.

P-072

High dose maintenance infliximab therapy in paediatric inflammatory bowel disease: clinical experience, safety and efficacy

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Objectives and Study: Inadequate response to infliximab (IFX) therapy in inflammatory bowel disease (IBD) may necessitate dose intensification. We evaluated safety and efficacy of high dose (HD) IFX [greater than 10mg/kg every 8 weeks] during maintenance therapy in pediatric IBD.

Methods: Electronic medical records were reviewed retrospectively for all pediatric IBD patients who received HD IFX any time during the maintenance period (after standard induction) between January 1st 2010 and July 1st 2018. Clinical, laboratory and demographic data were collected.

Results: 40 children received HD maintenance IFX for IBD at doses between 10 and 17.4mg/kg every 4 to 7 weeks. 75% male; 72% Crohn's disease (L1 0%, L2 44.5%, L3, 55.5%; B1 90%, B2 3%, B3 7%), 15% ulcerative colitis, 13% IBD unclassified (E1 9%, E4 91%, S1 28%, S0 72%). The median age at IBD diagnosis was 11 (IQR 4) and the median duration of diagnosed IBD at HD IFX initiation was 16.5 months (IQR 33). They were all anti-TNF naïve. At HD IFX initiation 2 (5%) patients were receiving corticosteroids and 27 (68%) were on concomitant immunomodulatory therapy (56% azathioprine, 45% methotrexate). The median IFX dose at time of HD IFX initiation was dose 7 (IQR 5). Median follow up post HD maintenance IFX initiation was 23.5 months (IQR19). Twelve weeks post initiation of HD IFX ,19/40 (47.5%) and 29/40 (73%) had clinical remission (PCDAI or PUCAI < 10) and response (≥ 20 drop in PCDAI/PUCAI) respectively. Clinical remission and response rates at week 52 post HD IFX initiation were 20/37 (54%) and 28/37 (76%) respectively. Clinical remission and response at week 72 were 19/33 (57.6%) 26/33 (78.8%). The median CRP was significantly higher at week 12 in those who ultimately discontinued therapy (20 vs. 5mg/l, $p=0.0003$) Median serum IFX trough levels increased significantly from 1.95 to 7.85u/ml ($p< 0.0001$). Median CRP decreased significantly from 11.9 at baseline to 5.8mg/l ($p=0.017$). Median fecal calprotectin decreased from 517 to 184ug/g ($p0.59$). At last follow up, IFX was discontinued in 5 (12.5%) due to loss of response. Dose de-escalation occurred in 20 (50%). There were no cases of serious infection or malignancy. One patient discontinued therapy due to IFX induced psoriasis.

Conclusion: HD IFX therapy may benefit paediatric IBD patients who have failed standard doses of IFX. In this cohort the majority of patients were able to continue therapy and de-escalation was possible in half of the patients. No new safety signals were identified.

Disclosure of Interest: SI, AF, KJ: Abbvie, Jansen

P-073

Effect of accelerated Infliximab induction on short term outcomes of paediatric acute severe ulcerative colitis

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Objectives and Study: Due to a higher inflammatory burden and a rapid clearance of Infliximab (IFX) in Acute Severe Ulcerative Colitis (ASUC), the accelerated IFX induction may be considered (IFX up to 10 mg/kg per dose, at week 0, 1 and 4-5) in those patients who need to start second line treatment. The aim of our study is to describe the short-term outcomes of ASUC pediatric patients who have received an accelerated IFX induction regimen in our Unit.

Methods: In a retrospective study we collected data from patients with ASUC who received treatment with accelerated IFX induction. We analyzed demographic, clinical and analytical data as well as treatment adverse events from medical records. The short-term outcomes (at the end of the induction and at 3 months) were analyzed based in the Paediatric Ulcerative Activity Index (PUCAI) and analytical parameters (haemoglobin, C reactive protein (CRP), erythrocyte sedimentation rate (ESR) and albumin).

Results: Six patients with ASUC who received accelerated IFX induction were included (5 male; median age at diagnosis 10.5 years (IQR: 2-15); mean time from diagnosis to ASUC flare: 1.8 years (IQR: 0-9 years)). At disease onset, 5/6 patients presented with pancolonic involvement (E4) with an average PUCAI of 55 points. At ASUC flare all the patients presented pancolonic involvement with a PUCAI over 65 points, 50% of them had anaemia, 66.6% elevation of inflammatory markers (CRP and / or ESR) and 50% hypoalbuminemia. The patients received an accelerated IFX induction with IFX at 10 mg/kg at 0, 1 and 4 - 5 weeks without adverse events. After accelerated IFX induction regimen 5/6 patients showed clinical response and normalización of lab tests (haemoglobin, inflammatory markers and albumin), with one patient failing treatment and needing surgery (colectomy rate 16.6%). At 3 months follow-up, no new patients needed colectomy. One patient had an infusional reaction and was changed to Vedolizumab treatment maintaining remission, the other 4 patients were maintained on IFX treatment (1 clinical remission, 3 mild clinical activity). The overall colectomy rate after accelerated IFX induction remained in 16,6%.

Conclusions: In our cohort of ASUC patients treated with an accelerated IFX induction regimen we observed an 83.3% free colectomy rate at short-term, being this regimen a valid therapeutic option to avoid surgery. Prospective and comparative studies are needed to determine the efficacy of this strategy in reducing the colectomy rate, both in the short and long term follow-up.

P-074

Is the Rapid Infliximab infusion a safe and cost saving strategy in paediatric Inflammatory Bowel Disease?

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Objectives and Study: Rapid Infliximab (IFX) infusion administered over 60 minutes is a safe strategy in selected Inflammatory Bowel Disease (IBD) adult patients. Some paediatric studies found similar results among children but data are still scarce. The aim of our study is to evaluate the safety of rapid IFX infusion strategy in our cohort of Pediatric IBD (PIBD) patients and analyze the impact of this strategy on health care resources.

Methods: PIBD children under IFX treatment using standard protocol (2 hour IFX infusion), and who had received at least 4 previous standard infusions, with no dose change in the last 2 doses, and without infusion reactions were switched to receive a 1-hour IFX infusions. Demographic and clinical data were collected from medical records, and patient and family satisfaction was recorded by telephone survey. The optimization of health care resources was also analyzed.

Results: A total of 46 PIBD patients were under IFX treatment during the study period (February 2018-February 2019) of whom 26 met inclusion criteria and were switched to rapid IFX infusions (14 Crohn's Disease (CD), 12 Ulcerative Colitis; 17 males). The mean age at switch was 15.3 years (IQR 5.3-17.9) with a mean time of IFX use of 30 months (IQR: 4-78). Sixteen patients were receiving concomitant immunomodulators. A total of 154 rapid IFX infusions were administered with a mean dose of IFX of 5.4 mg/kg (IQR 4-10) and an average frequency of 6.7 weeks (IQR 4-8). No patient received premedication at any time and no infusion reactions were seen during the study period. Family and patient satisfaction (22/26) was higher in rapid IFX infusion strategy than in standard protocol (9.1/10 versus 7.6/10). During the study period 154 hours of hospitalization were saved.

Conclusion: Rapid IFX infusion strategy in selected P-IBD patients is safe and well accepted by patients and their families. In addition, it is a cost saving strategy, minimizing the loss of work and teaching hours by the caregivers and patients, and allows optimization of the hospital resources. These results have led us to establish rapid IFX infusion in selected patients (with stable previous doses and no infusion reactions) as the standard protocol in our center.

P-075

Predicting the outcome of infliximab optimization after loss of response in pediatric IBD: a retrospective analysis of a reactive approach

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Objectives and Study: Therapeutic drug monitoring (TDM) is an established useful mean to manage loss of response (LOR) to infliximab, which occurs in approximately 30% of children. Very few studies have examined the impact of infliximab-therapy intensification based on trough levels and anti-drug antibodies (ATI) in children. Therefore, we aimed to evaluate the clinical outcome of such reactive approach in a pediatric cohort of patient with inflammatory bowel disease (IBD).

Methods: Trough levels of all children under scheduled infliximab therapy with LOR and who received dose intensification were retrospectively collected. ATI positive patients were excluded. Clinical remission, defined as a PUCAI < 10 and a wPCDAI < 12.5 at 6 and 12 months was the main outcome evaluated. Therapy optimization was performed through dose intensification, shortened dosing interval or both.

Results: Thirty-eight IBD children [22 (57%) Ulcerative colitis] were included in the study; mean PUCAI and wPCDAI at the time of LOR was 35±14 and 31±22, respectively. At 6 months, 21 patients (55%) reached clinical remission after dose intensification. At 12 months, 3 patients had discontinued infliximab and 20 of the 35 patients still under infliximab (57%) were in clinical remission. Trough levels below 1.37 µg/ml before dose intensification were best associated with 6-month clinical remission (AUC=0.70, p = 0.03, 78% sensitivity, 50% specificity), with 9/14 patients (64%) with baseline trough level < 1.37 µg/ml experiencing clinical remission versus 10/24 (41%) of patients with trough level >1.37 µg/ml (p=0.04).

Conclusion: Treatment intensification is effective in more than 50% of children experiencing secondary loss of response to infliximab. A pre-escalation trough level below 1.37 µg/ml makes this approach more likely to be successful.

P-076 (Poster of Distinction)

Infliximab clearance at and post induction predicts clinical and endoscopic outcomes at 1 year in children with Crohn's disease treated with Infliximab

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Objectives and Study: Infliximab Clearance (IFX-CL) is varied in children with Crohn's disease (CD), and CL is increased relative to body weight in those under 30kg at induction. Our aim was to determine if CL at and post induction can predict 1 year outcomes in children treated with IFX

Methods: IDEal study was conducted at 3 Canadian Children IBD Network sites. We prospectively followed 35 pediatric CD patients who initiated IFX. 88% required dose optimization. NONlinear Mixed Effects Modelling was used to develop a population PK model. 1 year follow-up data for 26 patients were available. Non-responders were defined as Weighted Pediatric CD Activity Index (wPCDAI)≥12.5, persistently elevated CRP>4, intestinal surgery, discontinuation of IFX, or steroid use during 6 months prior to 1 year follow-up. Fecal Calprotectin (FCP), ESR and Simple Endoscopic Score for CD (SES-CD) were also collected. Correlation analysis, Fisher exact test, and logistic regression were used to identify predictors of clinical, endoscopic and biomarker response at 1 year. ROC curve was used to estimate cut-off points for predicting a response

Results: The median follow-up was 12.8 months [11.8;14.98]. 20 patients were responders (11 males) and 6 non-responders (2 males). Age, weight and gender had no effect on 1 year outcomes. Of the 6 non-responders - 1 switched to a new class biologic, 1 remained on IFX, 4 required intestinal surgery (2/4 remained on IFX post intestinal resection), 21/26 patients had a follow-up colonoscopy and 13/21 achieved mucosal healing (SES-CD< 4). CL at doses 1 and 5 predicted clinical and endoscopic response at one year (p=0.03, r=0.474 and p=0.005, r=0.592, respectively). Dose 1 CL≥0.321L/day and Dose 5 CL≥0.305L/day were associated with poor outcome (AUC[95%]=0.78[0.56;0.99]) (AUC[95%]=0.99[0.66;1.00]) respectively. The non-responders had higher IFX trough at dose 5 comparing to the responders (10.1[7.3;13.5] and 4.9[3.4;7.4], respectively, p=0.028). All non-responders were dose optimized with median dose 6.0mg/kg[5.4;9.0] and frequency 4.3 weeks [4;6] at dose 5 as compared to 7.2mg/kg[6.9;7.8] and 6 weeks[4;6] in responders (p>0.1). wPCDAI< 12.5 at doses 4 and 5 predicted clinical response, with dose 5 being the better predictor(p=0.000,r=0.697). The odds of a dose 5 non-responder to respond at one year were 0.03 [0.02;0.39]. Dose 5 FCP≤221 mcg/g was a predictor of remission and mucosal healing (AUC[95%]=0.78[0.48;1.00]). FCP for non-responders were Dose 5-1140 mcg/g [219;2416], Year 1-518 mcg/g [152;1808]. FCP for responders were Dose 5-95 mcg/g [55; 343], Year 1-73 mg/g [28;276]

Conclusions: IFX-CL at dose 1 and 5 are predictors of clinical and endoscopic response in children with CD. Increased CL suggests inadequate response to IFX treatment. Low wPCDAI, CRP and FCP at dose 4 and 5 are also predictors of response. Similar to published study, FCP of ≤221mcg/g at dose 5 is the threshold for predicting clinical remission and mucosal healing. With dose optimization, IFX trough at dose 5 was no longer a predictor of better clinical or endoscopic outcome at 1 year. 1 year analysis indicates that with dose optimization at induction, the medium-term response to IFX can be predicted as early as Doses 4 and 5 and effort should be made to alter treatment earlier if inadequate response was observed

P-077

Secondary loss of response to TNF antagonist after stepping to monotherapy in paediatric inflammatory bowel disease

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Objectives and Study: Tumour necrosis factor (TNF) antagonists feature an effective treatment in IBD, however from 23 to 46% of the patients can show a loss of response (LOR) to anti-TNF during maintenance treatment. The most common cause is the immunogenicity against anti-TNF; the concomitant use of another immunosuppressant (IS) helps to maintain adequate drug levels and to prevent formation of antibodies against them. Our aim is to describe the secondary LOR (understood as clinical relapse or need for treatment intensification) after stepping to monotherapy in our paediatric IBD patients.

Methods: Retrospective descriptive study of IBD patients that, after receiving combined treatment (anti-TNF and thiopurines), stepped to monotherapy with Infliximab (IFX) or Adalimumab (ADA) from October 2012 to January 2019 or until transfer to an adult Unit. Demographic and clinical data, outcomes after stepping to monotherapy, evolution of drug levels anti-drug antibodies (at 3, 6 and 12 months), and LOR management, were collected.

Results: A total of 33 patients (28 Crohn's Disease, 5 Ulcerative Colitis; 60% males) stepped to monotherapy with anti-TNF during this period; 19 (58%) with Adalimumab, 14 (42%) with Infliximab. Median time of combined treatment before stepping to monotherapy was 18 months (range: 6-50 months). Before stopping thiopurines, patients were in clinical, endoscopic and biological remission. Median follow-up in monotherapy was 23.5 months (range: 1- 75 months). Six patients out of 33 (18%) experienced a secondary LOR to anti-TNF: 4 patients (66.6%) treated with IFX (1 UC, 3 CD) and 2 patients (33.3%) with ADA (2 CD). Four patients with LOR presented with a clinical relapse (2/4 with low drug levels), and in two sub-therapeutic drug levels were detected without symptoms. One of these patients showed positive antibodies against IFX. In 2 patients that presented with clinical relapse, a new endoscopy showed activity. After verifying secondary LOR, anti-TNF treatment intensification was done in all of the patients, with IS being reinitiated in 2/6 (one with antibodies against anti-TNF). After treatment optimization, five patients regained response (83%) as well as therapeutic drug levels. The patient that did not regained response showed clinical and endoscopic activity with adequate drug levels, so a change to a new biologic (ustekinumab) was done. The probability of failure with ADA in CD patients was of 10% and with IFX 30% ($p= 0.15$). A relation between clinical severity at diagnosis and LOR with monotherapy was not found ($p= 0.28$).

Conclusions: In this cohort we have observed a secondary loss of response to anti-TNF in 18% of the patients, inferior to the one described in the literature. In all cases treatment intensification was done, followed by reinitiation of immunosuppressive therapy. Treatment optimization was an effective strategy to regain response in the majority of our patients. No relation was found between secondary LOR and the anti-TNF used neither with the clinical severity at the time of the diagnosis.

P-078

Outcome of treat to target strategy in paediatric patients with Crohn's disease and ulcerative colitis on Infliximab

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Objectives and Study: Treat to target strategy has been proposed in adult IBD to improve quality of life, symptoms and to treat inflammation. There are little data in the paediatric population for this approach. The aim of this study was to look if set goals (reduced PCDAI/PUCAI and Mayo/SES-CD) were achieved in a group of paediatric patients who started treatment with Infliximab (IFX).

Methods: We conducted a retrospective analysis of children diagnosed with IBD who received IFX at our institution. Data from colonoscopy results were collected to evaluate mucosal healing: Mayo score for ulcerative colitis (UC) and SES-CD for Crohn's disease (CD). We also compared the data with activity scores (PUCAI and PCDAI), CRP and faecal calprotectin, (FC).

Results: A total of 61 patients were identified, 46 with CD (Group 1) and 15 with UC (Group 2). Age range: 3-15 years with a median age of 10 years. Males n=38. Group 1 consisted of 46 patients, 26 males. Age range was 0-15 years with a median of 9 years. SES-CD was assessed in all patients before starting treatment with IFX. The median score was 3 (range from 0 to 8). After 1 year of treatment, the SES-CD score dropped to a median of 1 with a range of 0-7 in 36 patients. The median value of FC before commencing treatment (n=37) was 2282 mg/kg (range: 133-6000 mg/kg) and at revaluation median FC (n=39) resulted 105 mg/kg (range: 15-6000 mg/kg). Median CRP pre-commencing IFX (n=42) was 12 mg/l (range: 5-167 mg/l) and after 1 year (n=42) it was 5 mg/l (range: 0.6-67 mg/l). PCDAI was found to be < 10 in 78% of the children with UC after 1 year follow up. Group 2 consisted of 15 children, 13 males. Age range: 4-13 years with a median of 10 years. Mayo score was evaluated in all patients prior to starting treatment with IFX (n=15). The median score was 2 (range 1-3). At follow-up (n=10) the median score dropped to 1 (range 0-3). FC median prior to starting IFX (n=13) was 1032 mg/kg (range: 23-3000 mg/kg) and decreased to 69 mg/kg (n=14) after 1 year (range: 15-1852 mg/kg). CRP pre commencing median (n=15) was 6 mg/l with a range of 5-19 mg/l and at revaluation (n=15) it was 5 mg/l with a range of 5-8 mg/l. PUCAI was found to be < 10 in 60% of the children with UC after 1 year follow up.

Conclusions: Our data suggest that set goals were achieved in CD and UC with a decrease of SES-CD and Mayo scores and with an improvement of both PCDAI and PUCAI scores. We suggest that paediatric patients get targets set at the beginning of their treatment and assess outcomes at set times.

P-079

Switching original infliximab to biosimilar seems safe in paediatric inflammatory bowel disease

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Objectives and Study: Infliximab is a very important option in the treatment of inflammatory bowel disease with moderate to severe activity. This biological agent is available in Europe since 1999. The use of the first biosimilar-infliximab (BS) was authorized in 2013 by the European Medicines Agency. The choice to switch drugs depends on economic factors, but mostly safety and efficacy profiles. We aim to characterize paediatric patients treated with originator-infliximab (OI) and compare the evaluation of response-rate with patients treated with biosimilar-infliximab.

Methods: We conducted a retrospective study of paediatric patients treated with infliximab having at least 11 months of follow-up after switch at a central hospital. Clinical status was determined by Paediatric Ulcerative Colitis Activity Index (PUCAI) and Paediatric Crohn's Disease Activity Index (PCDAI) scores. Laboratory response was assessed through quantification of faecal calprotectin (FC). Both clinical and laboratory evaluations were gathered at 6 and 12 months after the first infliximab treatment; and every 2 months after switching from OI to BS. Switch protocol selected stable patients on OI to be switched. Some patients started biological with BS.

Results: A total of 60 patients were studied, aged 4-19 years old (mean 16 years), 53% males, 88% with Crohn's disease and 12% with Ulcerative Colitis. There was no treatment switch in 73% of patients, (73% started BS and 27% on OI were not stable), with average treatment of 2 years. There was no statistical significance between PUCAI or PCDAI scores at 6 ($p=0.105$) and 12 ($p=0.78$) months between treatment groups. Also, there was no statistical significance between FC at 6 ($p=0.13$) and 12 ($p=0.37$) months. In the remaining 27% in sustained clinical remission, treatment was switched from IO to BS, with an average duration of 15 months after switch. There was no elevation of the PUCAI or PCDAI scores collected at 6 and 12 months after the switch. There was a transient elevation of FC in 75% of patients with statistical significance ($p < 0.05$). In this sub-group, we observed a mean FC of 59 $\mu\text{g/g}$ (SD 306,7 $\mu\text{g/g}$) at the switch time, with a progressive elevation during the first 4-6 months after switch (average FC 242 $\mu\text{g/g}$, SD 304,5), followed by a decrease during the next 6 months. This elevation did not affect activity indexes, all patients maintaining clinical remission throughout all follow-up period after switch.

Conclusion: Safety and response-rate to induction were identical in OI and BS. Switching from OI to BS does not seem to compromise the efficacy or safety of the biological agent, providing the same response with a better cost-effectiveness ratio. Despite the promising results, the complexity of the molecules and the concept of biosimilars require continuous clinical and laboratory monitoring of treatment.

P-080

Combination therapy of Adalimumab with an immunomodulator is not more effective than Adalimumab monotherapy in children with Crohn's disease: a post-hoc analysis of the PAILOT randomized control trial

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Objectives and Study: The PAILOT trial was a randomized controlled trial aimed to evaluate the effect of proactive vs. reactive therapeutic drug monitoring in children with Crohn's disease treated with adalimumab. Our aim in this post hoc analysis was to assess the efficacy and safety of combination treatment in comparison to adalimumab monotherapy at week 72 after adalimumab induction.

Methods: Participants were children 6-17 years old with moderate-to-severe Crohn's disease (n = 78), naïve to biologic treatment, who responded to adalimumab induction at week 4. Patients receiving immunomodulators at baseline according to their physician's discretion, maintained a stable dose until week 26; patients could then discontinue immunomodulators. At each visit (week 4, 8 and every 8 weeks thereafter till week 72) patients were assessed for pediatric Crohn's disease activity index, serum measures, fecal calprotectin, adalimumab trough concentration and anti-adalimumab antibodies.

Results: Out of the 78 patients (29% females; mean age, 14.3±2.6 years), 34 patients receive combination therapy and 44 patients receive monotherapy. Baseline characteristics at week 4 did not differ between groups. During the study period there was no significant difference in the rates of sustained corticosteroid free clinical remission (29/44, 66% vs. 22/34, 65%; p=0.9), and sustained composite outcome of clinical remission, CRP≤0.5 mg/dl and calprotectin≤150µgr/gr (14/44, 32% vs. 10/34, 29%; p=0.8) between the combination group and the monotherapy group, respectively. Adalimumab serum trough concentrations and immunogenicity were not significantly different between groups at all visits. The rate of overall and serious adverse events was similar in both groups.

Conclusions: Combination therapy of adalimumab and an immunomodulator is not more effective than adalimumab monotherapy in children with Crohn's disease.

(Clinicaltrials.gov no: NCT02256462).

P-081

Outcome of treat to target strategy in paediatric patients with Crohn's disease and ulcerative colitis on Adalimumab

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Objectives and Study: Treat to target strategy has been proposed in adult IBD to improve quality of life, symptoms and to treat inflammation. There are little data in the paediatric population for this approach. The aim of this study was to look if set goals (reduced PCDAI/PUCAI and Mayo/SES-CD) were achieved in a group of paediatric patients who started treatment with Adalimumab (ADA).

Methods: We conducted a retrospective analysis of children diagnosed with IBD who received ADA at our institution. Data from colonoscopy results were collected to evaluate mucosal healing: Mayo score for Ulcerative Colitis (UC) and SES-CD for Crohn's Disease (CD). We also compared the data with activity scores (PUCAI and PCDAI), CRP and faecal calprotectin, (FC).

Results: A total of 24 patients were identified, 20 with CD (Group 1) and 4 with UC (Group 2). Age range: 2-13 years with a median age of 9 years. Males n=14. Group 1 consisted of 20 patients, 13 males. Age range was 3-13 years with a median of 9 years. SES-CD was assessed in 9 patients before initiating treatment with ADA. The median score was 2.5 (range from 0 to 8). After 1 year of treatment, the SES-CD score dropped to a median of 1 with a range of 0-5 in 10 patients. The median value of FC before commencing treatment (n=15) was 574 mg/kg (range: 66-6000 mg/kg) and at revaluation median FC (n=18) resulted 108 mg/kg (range: 11-1491 mg/kg). Median CRP pre-commencing ADA (n=19) was 9 mg/l (range: 5-166 mg/l) and after 1 year (n=19) it was 5 mg/l (range: 0.3-8 mg/l). PCDAI was found to be < 10 in 70% of the children with CD after 1 year follow up. Group 2 consisted of 4 patients, 3 females. Age range was 2-10 years with a median of 5 years. Mayo score was evaluated in all patients prior to starting treatment with ADA (n=4). The median score was 2.5 (range 1-3). At 1 year follow-up (n=2) the median score was 0.5 (range 0-1). The median value of FC prior to starting ADA (n=3) was 1966 mg/kg (range: 217-3000 mg/kg) and decreased to 15 mg/kg (n=4) after 1 year (range: 15-1173 mg/kg). CRP pre commencing median (n=4) was 40 mg/l with a range of 8-81 mg/l and at revaluation (n=4) it was 5 mg/l with a range of 2-6 mg/l. PUCAI was found to be < 10 in 50% of the children with UC after 1 year follow up.

Conclusions: This study suggests that setting a target and monitoring SES-CD in CD and Mayo scoring in UC improves clinical outcomes (PCDAI and PUCAI), more in Crohn's disease than Ulcerative Colitis. Treat to target should become routine clinical management in paediatric IBD patients.

P-082

Reinduction for paediatric patients with loss of response to Adalimumab despite weekly interval dosing is only successful with concomitant immunomodulators

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Objectives and Study: Loss of response (LOR) to Anti TNF agents is a frequent occurrence in children treated with these medications for Crohn's disease. The goal of this study was to review our experience with two reinduction strategies for loss of response to adalimumab despite weekly dosing interval: Reinduction with methotrexate (R+M, used 2014-2016) and more recently, in an effort to reduce immune suppression, reinduction alone (2016-2019). In all cases patients continued weekly adalimumab.

Methods: Retrospective chart review. Only children who had obtained primary remission with adalimumab and subsequently developed LOR (clinical relapse or developed elevated calprotectin) that did not respond to weekly dosing for at least 8 weeks were included. Reinduction was either single dose (120-160 mg) or 160/80mg.

Results: We identified 22 cases (14 male) mean age was 14.6±4 years. Thirteen (59%) received R+M, 9(41%) received reinduction alone. Of these 9 patients, 6 had a clinical relapse and 3 received reinduction for elevated calprotectin and CRP despite clinical remission. All patients with reinduction alone had low trough levels without antibodies, ranging from 0 - 3.9 mcg/ml. Among children receiving R+M, clinical remission was obtained in 7/13(53.8%). Relapse occurred in 4/4 patients who decided to stop methotrexate 6-12 months later. Among patients receiving reinduction alone, remission or significant improvement in inflammation occurred in only 1/9 (11%) and all 9 (100%) received additional therapy or switched therapy due to clinical failure of reinduction.

Conclusions: Use of a reinduction regimen for pharmacokinetic loss of response to adalimumab was only successful in patients who received concomitant methotrexate.

P-083

Experience and outcomes in paediatric Inflammatory Bowel Disease (pIBD) on Vedolizumab with biomarker and Therapeutic Drug Monitoring (TDM)

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Objectives and Study: Vedolizumab (VDZ) is a humanized immunoglobulin G1 monoclonal antibody to $\alpha 4\beta 7$ integrin which blocks gut lymphocyte trafficking. It is an effective induction and maintenance therapy for Ulcerative Colitis (UC) and Crohn's disease (CD). Paediatric use in IBD is off label; therefore data involving paediatric populations are encouraging but still limited. The aim of this study was to look at outcomes of patients treated with VDZ, especially in regards to TDM.

Methods: Retrospective review of patients with UC and CD treated with VDZ in our centre over a 2 year period. Clinical activity scores (PCDAI/PUCAI/PGA), laboratory parameters, endoscopic and histological information were collected for at least one year after initiation of VDZ treatment.

Results: At initiation of treatment 15 patients with CD: n=8 and UC: n=7, Female n= 8, age range: 5.9 years-17.9y (median 13.58 y). The indication to start VDZ was failure of 2 anti-TNF treatments; all patients had either Infliximab or Adalimumab or both.

Patients with CD had an increase in mean Hb from 116 mg/dl to 127.67 mg/dl (p: 0.14); with UC patients from 114.2 mg/dl to 128.2 mg/dl (p: 0.056).

Patients with CD increased mean Albumin from 38.83 mg/dl to 40.17 mg/dl (p: 0.082), while in UC mean Albumin increased from 42 mg/dl to 44 mg/dl (p: 0.468).

Calprotectin level in CD of < 100 mg/kg was achieved in 1/8 patients (12.5%), < 200 in 2/8 (25%), the remaining 5/8 (62.5%) had levels of 220 to 5300. In UC level of < 100 mg/kg was achieved for 3/7 patients (42%), < 200 1/7 (14%), the remaining 3/7 (42%) had levels of 1043 to 2996.

8/15 (53%) patients had endoscopies prior to switch to VDZ (CD n=5 , UC n= 3), 10/15 (66%) had scopes within one year after VDZ (CD n= 7/8 (87.5 %) UC n=3/7 (42%)). All CD patients on VDZ had macroscopic/histological findings of active disease. VDZ was stopped in 3/8 (37.5 %) CD patients 5-9 months into treatment due to poor clinical response. The remaining 5/8 (62.5 %) remained at least one year on VDZ under on-going review. 3/7 (42%) UC patients on VDZ who had scopes continued to have macroscopic and histological inflammation. VDZ was stopped in one UC patient after 9 months due to no response to treatment.

PUCAI pre VDZ was 15 to 55 (mean: 38.57), post VDZ 0-50 (mean: 11.42) (p: 0.005), 1/7 did not drop PUCAI. PCDAI pre VDZ was 10-65 (mean: 41.56), post VDZ 7.5-75 (mean: 28.13)(p: 0.192)

Drug levels in UC patients (5/7) at the start of VDZ treatment were between < 3.1-59.6 mg/L (mean: 22.2), 6-12 months into VDZ treatment 7.5-18.9 mg/L (mean: 9.6). Drug levels in CD patients (6/8) were initially between < 3.1-26.5 mg/L (mean: 16), dropping to < 3.1-11.5 mg/L (mean: 8.5).

Conclusion: Our results suggest that Vedolizumab can be an effective treatment for paediatric patients with IBD, previously not responding to treatment with anti TNF α biologics, however, outcomes were better in Ulcerative Colitis patients. Multicentre prospective studies should improve our knowledge and experience.

P-084

Dose interval intensification of Ustekinumab is effective in paediatric Crohn's disease with post-operative recurrence refractory to Ustekinumab every 8 weeks

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Objectives and Study: An increasing number of children with Crohn's disease (CD) are developing multi biologic refractory disease. This is particularly significant in patients who have already had a resection during childhood and now have post operative recurrence with disease. Ustekinumab (anti P40) is being increasingly used as a third line therapy in patients refractory to two biologics or with pharmacodynamics failure. Here we report our experience with ustekinumab.

Methods and Results: 4 adolescents aged 17-19 received dose interval intensification with follow up ranging 4-5 months . Previous surgeries appear in the table below. All four had received and failed anti TNF and combination therapy for post operative recurrence, all four had been switched to ustekinumab. One had obtained remission, one response, and two deteriorated as primary non responders (one with new bowel obstruction and 30 cm of severely inflamed neoterminal ileum, the other developed a new rectovaginal fistula).

All four escalated therapy to 90 mg q 4 weeks (from week 10 to week 52 after IV induction) ,all were in remission 4 months later. The patients with the vaginal fistula demonstrated closure of the outer orifice.

Conclusions: Q 4 week dosing of ustekinumab therapy led to remission in primary non responders and those with loss of response. We also witnessed closure of a rectovaginal therapy with this regimen

Gender/age Paris

Classification Surgery Previous

Therapy Ustekinumab

Response q 8 weeks Ustekinumab

Response q 4 weeks Labs

M /18 yrs L3L4B3p Ileostomy

Colectomy IFX ADA MTX Response

Not remission Clinical remission CRP down from 42 to 7

F/ 17 yrs L1B2 Ileocecal

resection ADA, IFX MTX Remission

Calprotectin still >500 Clinical remission Calprotectin 550 to 156

CRP normal

F/17 yrs L3B3 Ileostomy

Colectomy IFX AZA

ADA MTX No remission

New vaginal fistula after second injection Clinical remission

Closure vaginal fistula ESR 76 to 18

Alb 3.8 to 4.4

F/19 yrs L1B2 Ileocecal

resection ADA No remission

New Bowel obstruction Clinical remission with a mild relapse Calprotectin 1700, CRP unchanged 20

P-085

The surgical management of paediatric inflammatory bowel disease - a review over 5 years

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Introduction: Infliximab and Adalimumab are able to induce clinical and biological remission in patients with moderate and severe Crohn's disease (CD) and ulcerative colitis (UC). These therapies have led to a shift in management from controlling clinical symptoms to preventing disease progression. However, despite these advances in medical therapy, surgery is still required in 30%-40% of adult patients with CD and 20%-30% of adult patients with UC at some point during their lifetime.

Objectives: Review the indication, incidence and outcomes of children with IBD undergoing surgical intervention from a single centre.

Subjects and Methods: A retrospective case note review was undertaken on all patients with IBD over 5 years (2013-2018). We included all patients managed up to and including 18 years of age and reviewed the duration on medical management, indications for surgery, surgical procedures performed and outcomes following surgery.

Results: 20 patients were identified that required surgical input over the 5 year period (14 males, 6 females). Diagnosis was confirmed as CD in 13 patients and UC in 7 patients with median age of 11 years (range 2-15 years) at diagnosis. Median age at surgery was 14 years in CD (range 11-18 years) and 14.5 years in UC (range 5-17 years). All patients with UC were on Methotrexate, Infliximab or Adalimumab at the time of surgery. All patients with luminal CD were on Biological therapy. Rationale for surgery included refractory disease or failed medical management with on-going symptoms (4 patients: CD, 7 patients: UC), perianal fistula (2 patients: CD), stricturing disease (2 patients: CD), subacute bowel obstruction (2 patients: CD), acute abdomen (2 patients: CD) and acute perianal disease (1 patient: CD). 59% (10/17) of the abdominal surgeries were performed open (laparotomy) and 41% (7/17) were laparoscopic, the majority undertaken by a paediatric surgeon. 2 patients had been transitioned to adult care at the time of referral for surgery. Procedures performed included: 10 subtotal colectomy and ileostomy (7 for UC, 3 for CD), 5 right hemicolectomy and anastomosis (all for CD), 1 defunctioning loop colostomy (CD), 1 single incision laparoscopic surgery (SILS) for jejunal resection and anastomosis (CD), 2 EUA and insertion of seton (both in CD) and 1 EUA and excision of perianal skin tag (CD). Complications were documented in 7/20 (35%) patients; these included 1 anastomotic leak, 1 port site hernia, 2 superficial wound concerns, 2 hospital acquired pneumonia and 1 small bowel obstruction. At time of follow up 8/16 patients are documented as being off all medical therapy (4 patients with CD, 4 patients with UC). 8 patients are on medical therapy of which 4 patients have required further biological therapy (infliximab, adalimumab or vedolizumab).

Summary and Conclusion: The need for surgical intervention in PIBD commonly occurs peri-transition. It would therefore be important to involve adult surgeons in the decision making process when planning surgery in PIBD. Laparoscopic bowel surgery for IBD is emerging as the preferred intervention when second/third line medication has failed. It is important to be aware of the rates of surgical morbidity. This may be contributed by the cumulative effect of immunosuppressant therapy at the time of surgery.

P-086

Risk factors for stoma-related obstruction after ileal pouch-anal anastomosis in pediatric patients with ulcerative colitis

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Objectives and Study: Covering loop ileostomy is usually constructed for preventing anastomotic leak at ileal pouch-anal anastomosis (IPAA) in patients with ulcerative colitis (UC). Several reports have described that covering ileostomy sometimes causes small bowel obstruction after surgery for UC. We aimed to evaluate the risk factors for stoma-related obstruction (SRO) in pediatric patients with UC undergoing IPAA.

Methods: A retrospective review was performed using admission data from 2001 to 2018. Pediatric patients who underwent IPAA with covering ileostomy were evaluated for an association between SRO and perioperative factors. The diagnosis of SRO was defined as bowel obstruction around ileostomy and symptom relief by catheter intubation through the proximal stoma.

Results: Overall incidence of SRO for the 44 patients enrolled in this study was 36.4%. The comparison of perioperative factors between the patients with SRO and without SRO showed that patients complicated SRO had significantly lower average body mass index (BMI) (15.8 vs 19.1, $p=0.005$). The optimum cut-off point of BMI to predict SRO, based on receiver operating characteristic curve, was 17.1 (AUC: 0.76). The incidence of SRO in the patients with a BMI below 17 was significantly higher than that in the patients with a BMI of 17 or above (52.0% vs 15.8%, $p=0.01$). Other factors did not affect the occurrence of SRO.

Conclusions: Low BMI may be significant predictive factors for SRO after IPAA with covering ileostomy in pediatric patients with ulcerative colitis.

P-087

Surgical care of paediatric inflammatory bowel disease patients based on a prospective, nation-wide inception cohort registry (HUPIR)

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Objectives and Study: About one third of all paediatric inflammatory bowel disease (IBD) patients require surgical intervention within five years after the diagnosis. The complication rates after bowel resection and colectomy are lower in surgical centres with greater experience, however, there are only few prospective, epidemiological studies evaluating surgical management in paediatric IBD. Our aim was to evaluate the characteristics of surgical intervention in paediatric patients with IBD on a prospective, nation-wide manner based on the national inception cohort registry (HUPIR).

Methods: Newly diagnosed paediatric patients with IBD (ages 0-18 years) were registered and followed-up in this prospective, nation-wide inception cohort registry (HUPIR). The questionnaire includes epidemiological data, disease extension, disease activity and initial therapy at the time of registration. The follow-up questionnaire consists of questions about disease activity and therapy (medication and surgery). Patients who were registered between 01.01.2010. - 31.12.2015. and have been followed-up for at least 1 year were involved to evaluate the surgical practice in Hungary. The urgency of the interventions, the experience and specialty of the operating surgeon (pediatric vs. general) were analysed. Descriptive statistical methods were applied for data analysis.

Results: Between 2010 and 2015 827 children were registered (Crohn's disease (CD): 536, ulcerative colitis (UC): 237, IBD-U (unclassified):54). From the 827 patients 92 had surgical intervention (12%) (CD, 87, UC, 4, IBD-U,1). The cause for surgical intervention was perianal disease in almost half of the operated CD patients (48%, 44/87). Only 36% of all operations on CD patients (33/87) was bowel resection and 5 patients had intraabdominal complications requiring surgical intervention. Interestingly, only 3 UC patients (2%) had colectomy (3/237). About one third (31%, 18/59) of the interventions were urgent surgical cases. Two-third of the cases (63%, 34/54) was operated by a paediatric surgeon. Ten years (or more) of surgical experience was found in 78% (38/49).

Conclusion: Data of our prospective, nation-wide registry showed the frequency of surgical intervention in CD was similar to according international data; colectomy in UC was less common, however. Perianal disease was the most common reason for surgery in CD. The vast majority of surgical interventions were performed by paediatric surgeons.

P-088

Use of Leukocytapheresis in inflammatory bowel disease in paediatric patients. A serie of 7 cases

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Objectives and Study: Inflammatory bowel disease (IBD) cause outbreaks with an increase of granulocytes and monocytes activated. Leukocytapheresis (LCA) is a safe technique that has shown efficacy in ulcerative colitis. The technique is to replace activated leukocytes from the peripheral blood and, in consequence, decreasing the cytokines which are involved in inflammatory response. Objectives of this report is to describe the main characteristics of patients in whom LCA was made and evaluate the response to treatment, different types of LCA guidelines used and possible side effects during treatment.

Methods: A descriptive and retrospective study that analyse clinical and analytical data of patients diagnosed with IBD (according to the ECCO and ESPGHAN criteria) who underwent LCA a cause of refractory to conventional treatment, immunosuppression and biological treatment in a tertiary paediatric hospital between 2006 and 2018.

The following variables were studied: Demographic data, treatments received, clinical situation (PUCAI score) and blood analysis (at the beginning, during, at the end and one month after the LCA), the characteristics of the sessions, as well as the side effects that have taken place.

Results: Seven patients (3 women and 4 men) diagnosed with refractory ulcerative colitis were included. All of them had received previous treatment with corticosteroids, salicylates and/or Thiopurines. In addition 5 patients had been treated previously with Adalimumab and 2 with Infliximab. The major indication to initiate treatment with LCA was steroid dependence and/or loss of response to Adalimumab.

A total of 12 treatment cycles are analysed. The average duration of the cycles was 2 months (mean of 9 sessions per cycle). The sequence of sessions was 3 to 4 sessions weekly and then fortnightly. Each apheresis lasted 60-120 minutes at a flow rate of 30ml/min. The only adverse effect recorded was the elevation of blood pressure in one of the patients referred after the end of one session and local inflammation around the catheter which was observed in another one.

The reasons to finish LCA sessions were: 33% of cases due to treatment failure, 8% due to anaemia and 51% for clinical improvement that allowed decrease or withdrawal steroids.

In 56% of cases, a decrease in the PUCAI score of 20 points was observed at the end of the LCA and 2 patients presented a PUCAI 0.

We observed a decrease in total leukocytes in 58%, neutrophils in 67%, lymphocytes in 17% and monocytes in 42% of cases. 17% of patients had decrease of red cells without requiring transfusions. In 33% a decrease in the C reactive protein (CRP) was observed, the erythrocyte sedimentation rate (ESR) in 50% of the patients and faecal Calprotectin (FC) was determined in 7 of the 12 cycles, with an decrease observed of 90%.

Conclusion: In our experience, LCA has proven to be a safe and effective treatment in more than 50% of paediatric patients with refractory CU. The main outcome is the decrease of PUCAI score and acute phase reactants such as CRP, ESR and FC.

P-089

Follow-up of body height and weight changing in paediatric inflammatory bowel disease - monocentric retrospective study

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Objectives: Impairment of growth and failure to thrive are one of the most significant complications of inflammatory bowel disease (IBD) in paediatric patients. Decreased appetite, abdominal symptoms, malabsorption, growth hormone resistance, and genetic factors are the main factors which contributes in growth faltering and malnutrition. Pre-pubertal onset Crohn disease (CD) has a higher risk of growth failure, and final adult height is usually lower than of healthy controls. Several IBD treatments improve patients' growth and nutritional status. Avoiding corticosteroids, achieving deep remission, good patient compliance are important to maintain optimal growth in patients with paediatric onset IBD.

Study: Growth and weight gain from diagnosis and follow-up to evaluate the effect of time of diagnosis (pre or postpubertal) and favourable effect of different treatment modalities were investigated in paediatric IBD patients with CD and ulcerative colitis (UC).

Results: Impairment of growth (HFA Z-scores < - 2) was recognized in 9.75% of patients at diagnosis (4/41), 12.19% (5/41) were undernourished by body weight and 4.9% (2/41) by BMI (WFA/BMI Z-score < - 2) at the same time. At the end of the study or at the age of 18 years, 4.8% of patients (2/41) were undernourished. Both had CD, one had ascending hereditary spastic paralysis with feeding difficulty, other's compliance was insufficient. Two CD patients final height was lower, than expected. Diagnosis was before puberty in 7 cases Pre- or postpubertal onset of IBD and the different therapies (corticosteroids, exclusive enteral nutrition, immunosuppressants and biologics) had no significant effect on WFA, HFA and BMI Z-scores data.

Conclusion: Impairment of growth and malnutrition are important markers of activity of the disease, and have impact on quality of life. Most optimal therapy of IBD supports growth and weight gain, however, in some children it is ineffective. In these cases targeted therapeutic strategies are recommended.

Disclosure of Interest: Gabor Veres is supported by Abbvie and Nestle.

P-090

From Paris to Montreal: evolution of Crohn's disease from childhood to adult life-a long-term cohort study from the biologic era

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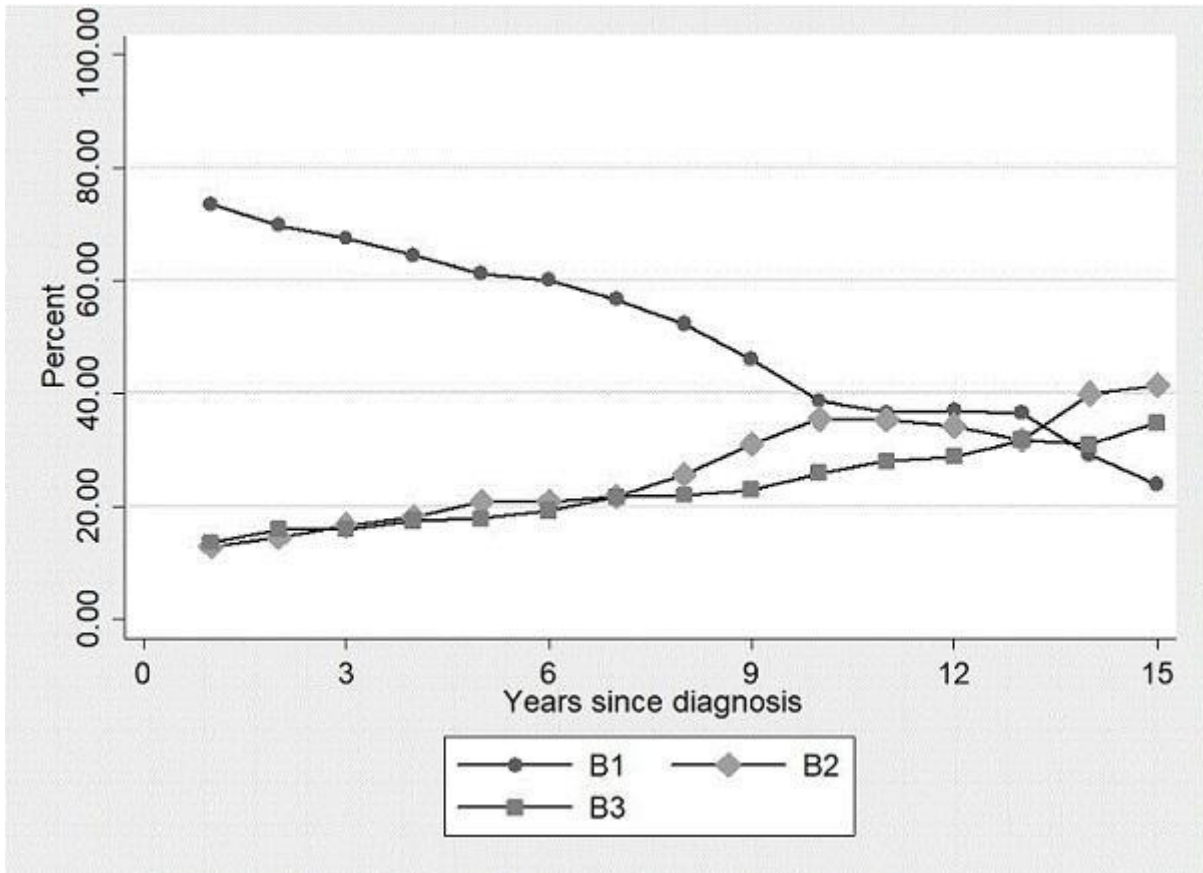
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Objectives and Study: Pediatric Crohn's disease (PCD) often presents with extensive and a frequent pan-enteric phenotype at onset. However, its long term evolution in to adulthood, especially since the widespread use of biological agents, is not well characterised. We conducted a single centre cohort study of all PCD patients transitioned to adult care to assess the long term disease evolution in the era of biologic therapy.

Methods: We conducted a retrospective observational, study of all PCD patients who were subsequently transferred to the care of an adult gastroenterology unit and had a minimum follow up of 2 years. We examined the case notes for evolution of disease location and behaviour. Disease location and behaviour was characterised using Paris classification at diagnosis and Montreal classification at last follow-up. In addition, we examined variables associated with complicated disease behaviour and the need for CD related intestinal resection.

Results: In total, 132 patients were included with a median age at diagnosis of 13 (IQR 11-14) and a median follow up of 11 years (range 4-14). At diagnosis, 23 (17.4%), 39 (29.6%) and 70 (53%) patients had ileal, colonic and ileocolonic disease. In addition, 31 (23.5%) patients had L4a or L4b disease at diagnosis (proximal or distal to the ligament of treitz respectively) and 13 patients (9.8%) had both whilst 27 (20.4%) patients had perianal disease. At diagnosis, 27 (20.4%) patients had complicated disease behaviour but 83 (62.9%) of patients had an extensive 'pan-enteric' phenotype. Of these patients only 55 (66.3%) retained the pan-enteric phenotype at last follow-up ($p=0.0002$). Disease extension was noted in 25 (18.9%) of patients and regression was noted in 47 (35.6%) of patients. whereas upper GI disease was noted in significantly fewer patients at last follow-up (21, 15.9%) ($p=0.0001$). More patients had complicated disease behaviour (46 patients, 34.9%, $p=0.0018$). There was a high exposure to both thiopurines 121 (91.7%) and biologics 84 (63.6%). The cumulative probability (95% CI) of surgery was 0.05 (0.02, 0.11) at 1 year, 0.17 (0.11, 0.24) at 3 years and 0.22 (0.15, 0.30) at 5 years. Neither disease location nor behaviour were associated with the need for intestinal resectional surgery.

Conclusions: Over the course of an extended follow-up period, there appeared to be changes in both disease location and behaviour in PCD. Interestingly, a significant proportion of patients had disease involution which may be related to a high rate of exposure to thiopurines and biologics. We were unable to identify any variables associated with complicated disease course or the need for intestinal surgery.



[Crohn's disease behaviour at diagnosis and last follow-up. A significant change in disease behaviour]

Disclosure of Interest: SS has received speaker fee from MSD, Actavis, Abbvie, Dr Falk pharmaceuticals, Shire and received educational grant from MSD, Abbvie, Actavis and is an advisory board member for Abbvie, Dr Falk pharmaceuticals, Janssen and Vifor pharmaceuticals. MKHA has received speaker fees from Abbvie, and travel grants from Abbvie, Dr Falk pharmaceuticals, MSD/Janssen and Nutricia. CT has received speaker fees from Abbvie, Sanofi, Nestle and travel grants from Abbvie, MSD, Nutricia.

P-092

Predicting severity and complications in pediatric Crohn's disease patients using vitamin D levels

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Objectives and Study: Pediatric Crohn's disease tends to be more aggressive as 80% will require surgery due to disease complications, 50% will require surgery within 10 years from diagnosis. The goal of this prospective study was to evaluate the role of vitamin D levels as a possible biomarker, influencing disease severity and predicting future complications and the need for surgery.

Methods: A prospective observational study, designed to prognosticate newly diagnosed pediatric CD in over 300 children aged 4-17 years from 17 sites in Europe and Israel over a 5-year period of which 3 year for enrollment and two years of follow up. This study was planned to evaluate outcomes related induction of first remission and the effect of initial therapy on these outcomes, to evaluate the correlation between various biomarkers and relapse by 78 weeks and complications and the need for surgery by 104 weeks.

Results: More than 300 patients were enrolled in this study, of which 219 had initial vitamin D level measurements. Most of the patients were males, and the average age was 12.9 ± 3.4 years. 76% of the patients had low vitamin D level at week 0 (defined as vitamin D < 20ng/ml). Persistent vitamin D deficiency (defined as vitamin D < 20ng/ml at week 0 and week 12 after therapy) was present in 59.6% of patients who had an initial low vitamin D at baseline. During long term follow-up, relapse (defined as an active disease PCDAI>10) occurred in 92 patients (42%) after 78 weeks. Relapse was not associated with either baseline or week 12 vitamin D levels ($p=0.194$ and $p=0.492$, respectively). Complications were defined as either fistula, stricture, abscess, or the need for surgery occurred in 59 (27%) of patients.

Conclusions: In this study we investigated whether serum vitamin D levels can predict and therefore be used as a biomarker for the prognosis of CD in newly diagnosed pediatric patients. Baseline vitamin D levels were not helpful for prognostication. However, low vitamin D at week 12 was a significant and independent predictor for the need of surgery.

P-093

A prospective study examining non-invasive proxies in predicting endoscopic disease activity in paediatric Crohn's disease

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Objectives and Study: Inclusion of surrogate markers such as serum CRP and faecal calprotectin (FC) with Paediatric Crohn's disease activity index (PCDAI) improves prediction of endoscopic activity in Crohn's disease (CD). A recently validated mucosal inflammation non-invasive index (MINI) score utilising stool frequency, CRP/ESR and FC demonstrated 87% specificity and 84% sensitivity in predicting mucosal healing in CD. ¹We aimed to validate MINI-index in our prospective cohort study.

Methods: In this prospective observational cohort study (ACTRN1261800074120), children (< 17 years) with complete ileo-colonoscopy at diagnosis or during follow up with paired PCDAI, CRP/ESR and FC within two weeks, were recruited from two participating children's hospital. Endoscopy scores were measured using Simple Endoscopic Score (SES-CD) score, remission was defined as SES-CD (0-3), mild activity (4-10) and moderate-severe activity >10. Endoscopic video were evaluated by an independent blinded review.

Results: A total of 70 children were recruited, 14 were excluded (3 with extensive proximal small bowel CD, 6 with incomplete colonoscopy, 5 FC not available < 2 weeks). Of 56 (34 males) included (n=17 had SES-CD 0-3), n=16 (SES-CD 4-10), n=23 (SES-CD >10). Mean(SD) SES-CD scores were 8.8 ± 8.3. Mini-index < 8 has sensitivity of 70% and specificity 90% in predicting endoscopic remission (SES-CD, 0-3).

Conclusions: In our prospective validation study, we report marginally higher sensitivity of MINI < 8 over FC cut off 300µg/g in predicting endoscopic remission. While our results suggest a high negative predictive value but a lower positive predictive value compared to recently published validation study. Further data is required before we use Mini-index to modify our treatment decisions.

References: 1. Cozijnsen MA, Ben Shoham A, Kang B, et al. Development and Validation of the Mucosal Inflammation Non-invasive Index For Pediatric Crohn's Disease. Clin Gastroenterol Hepatol. 2019 Apr 10.

Biomarker	PCDAI<10 (n=22/56)	CRP<5mg/L (n=12/56)	FC<300 µg/g (n=14/56)	Mini-index<8 (n=16/56)
Sensitivity	64.7%	53%	65%	70.6%
Specificity	71.8%	92.3%	92%	90%
Positive predictive value	50%	75%	78%	75%
Negative predictive value	82%	81%	86%	87.5%

[Biomarkers Cut off for defining endoscopic remission (simple endoscopic score =0-3)]

P-094

Characteristics of body composition, improving physical activity and social functioning in patients with paediatric Crohn's disease, while patients with ulcerative colitis are balanced from the beginning

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Objectives and Study: Characteristic symptoms of inflammatory bowel disease (IBD) are abdominal pain, malnutrition, weight loss and fatigue leading to altered body composition (BC), impaired physical activity (PA) and quality of life (QoL). The aim of this study was to answer the question, how does body composition, PA and QoL change in the first 6 months following diagnosis.

Methods: All in all 48 newly diagnosed IBD patients (Crohn's disease (CD): 31, ulcerative colitis (UC): 17) were enrolled in this study, from which 17 CD (mean age: 14.14±1.81ys, 9 male) and 10 UC (mean age: 14.18±1.95ys, 4 male) patients were involved in the final statistical analysis. Three study visits were conducted: at diagnosis (M0), two months (M2) and six months (M6) following diagnosis. At each visit height, weight, BC, PA and QoL were assessed alongside clinical assessment. Sex, gender and BMI based zscores were calculated from healthy control's BC data (n=307, mean age: 14.28 ± 2.1) via the LMS method.

Results: In CD group, weight (p< 0.05), BMI (p< 0.005), fat free mass (FFM) (p< 0.05) and total body water (TBW) (p< 0.05) z-scores were statistically lower at M0. FFM and TBW improved to M2 (p< 0.05), while weight and BMI restored to M6. UC patient's BC data were in normal range through the whole study period. At M0, UC patients had more positive body image. Bowel symptoms improved to M6 in both patient's group. Social functioning and PA raised in CD patients. PA was lower both in CD and UC patients at M0 and M2 compared to controls, which difference disappeared to M6.

Conclusion: According to our data, BC, PA and social functioning restores in 6 months after diagnosis in CD children. UC patient's BC data are normal at diagnosis as well.

P-095

Longitudinal follow up of body mass index as a predictor for severe disease course in children with inflammatory bowel disease

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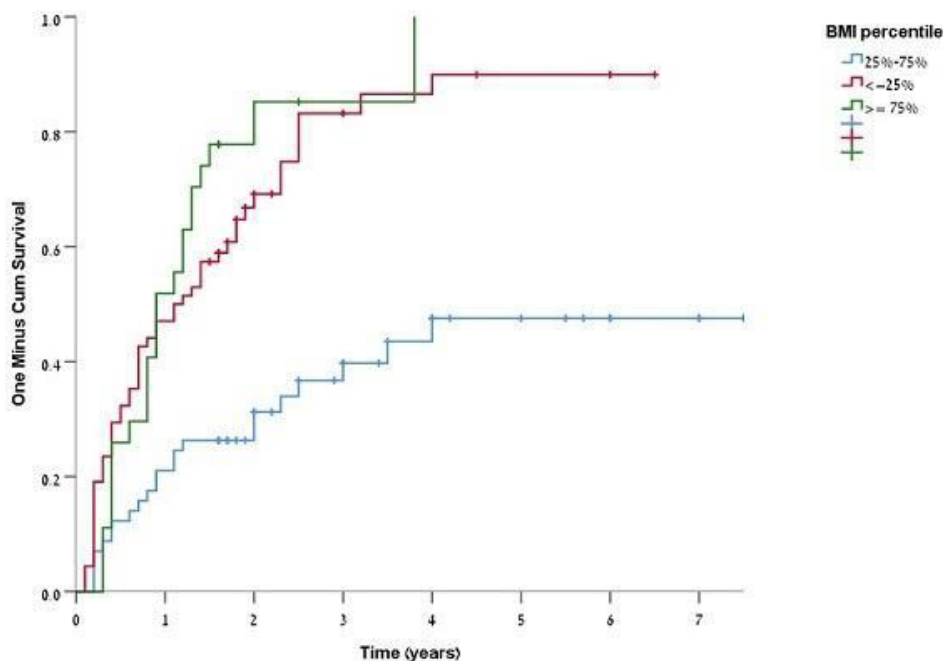
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Objectives and Study: Recent studies have shown that obesity may be associated with severe disease course in inflammatory bowel disease (IBD). The aims of this study were to present the longitudinal course of height, weight and body mass index (BMI) in children with IBD and to describe the impact of BMI on the clinical course of the disease.

Methods: We reviewed the medical records of children with IBD from the database of our pediatric gastroenterology center between 6/2010 and 08/2018. Anthropometric data were longitudinally collected every 6 months as were disease characteristics, course and therapy. Patients were categorized in quartiles according to BMI percentile.

Results: Of 152 children, 85 had Crohn's disease (CD) and 67 had ulcerative colitis (UC). The median age (IQR) at diagnosis was 14 (12-15.5) years. During a median (IQR) follow up of 2.95 (1.73-4.5) years, height Z-scores in the study population have not significantly changed. Weight and BMI Z-scores increased in the first 18 months since diagnosis in CD ($p < 0.001$) and UC ($p = 0.021$). BMI in the lower and upper quartiles at diagnosis was associated with higher risk of hospitalization (HR=2.72, $p = 0.021$). BMI in the lower quartile at diagnosis and at 6, 12 and 18 months was associated with higher risk of disease exacerbation (HR=3.25, 2.18, 2.01, 2.50, respectively, $p < 0.013$). BMI in the upper quartile at diagnosis and at 6 and 12 months was associated with higher risk of disease exacerbation (HR=3.98, 2.98, 2.39, respectively, $p < 0.012$). In a multivariate analysis, BMI in the lower and upper quartiles at diagnosis was associated with higher risk of disease exacerbation (HR=2.36 and 2.59, respectively, $p = 0.006$).

Conclusion: BMI in the lower and upper quartiles 18 months since diagnosis was associated with more severe disease course in children with IBD. The results support using BMI as a predictor of IBD course and prognosis.



[IBD exacerbation by body mass index at diagnosis]

Disease course of pediatric ulcerative colitis during follow-up; a prospective registry study of Japanese pediatric IBD patients

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Objectives and Study: The aim of this study was to elucidate the disease course of Japanese pediatric ulcerative colitis (UC) in the era of biological therapy.

Methods: Information was collected from JPIBD-R; a prospective registry study of newly diagnosed Japanese pediatric inflammatory bowel disease (IBD) patients from 2012. Clinical characteristics and therapeutic managements of pediatric UC patients during follow-up were analyzed. We excluded the patients with follow-up less than 1 year or an incomplete data.

Results: A total of 194 children with UC were analyzed. 94 [48%] children were female. Mean age at diagnosis was 11.8 years [range; 1.6-17.3 years]. Mean follow-up period was 3.0 years [range; 1.0-6.5 years]. A family history of IBD within 2nd degree was present in 25 [13%] children. At diagnosis, 148 [78%] children had pancolitis and 54 [28%] children had severe UC (pediatric UC activity index ≥ 65). During follow-up period, 19 [9.8%] children had episodes of extra-intestinal manifestations, and 30 [16%] children underwent colectomy. 146 [75%] and 102 [53%] children had received corticosteroid and immunomodulators (IMs), respectively. 60 [31%] and 71 [37%] children were treated with oral tacrolimus and biologic therapy (infliximab, adalimumab and golimumab in 51, 33 and 5 patients). 94 [48%] of all patients were treated with oral tacrolimus or biologic therapy. Oral tacrolimus was used as an induction therapy in short time in most cases. After oral tacrolimus therapy, 21 [35%] of 60 children required biologic therapy, and 23% [38%] experienced colectomy within follow-up period. However, 13 [21%] of 60 children could keep sustained clinical benefits with 5ASA, IMs or/and herbal medicines, which consist of indigo naturalis. 34 [67%] of 51 children treated with infliximab received IMs as combination therapy. Infliximab was used more than 1 year in 43% of children treated with infliximab. Infliximab was used for longer periods if it was used as combination therapy with IMs compared to monotherapy ($P < 0.05$).

Conclusion: Clinical characteristics of Japanese children with UC in this registry were similar to that of Western Europe. About a half of Japanese UC children were treated with oral tacrolimus or biologic therapy. The role of oral tacrolimus and biologic therapy in children with UC needs to be evaluated further.

P-097

The development and validation of a self-management skills assessment tool for children with Inflammatory Bowel Disease: the IBD-Skills Tasks and Abilities Record (IBD-STAR).

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Objectives and Study: For children with Inflammatory Bowel Disease (IBD), the development of self-management (SM) skills should begin far in advance of the transition period in order to achieve better disease outcomes. SM skills should be routinely measured, but existing SM assessment tools focus on transition and self-efficacy. A novel tool was therefore developed to measure the allocation of responsibility for SM skills for children with IBD using a content synthesis of existing tools, followed by a content validation process with an expert team. The tool was called the IBD-Skills Tasks and Abilities Record (IBD-STAR). The aim of this study was to assess the validity and reliability of IBD-STAR using a triangulation of data sources and methodologies to assess the accuracy of its reports. IBD-STAR contains eighteen scored items divided in five sections, each item details a SM skill with a scale for children to report if they can do this on their own (score two), with help (score one), or not at all (score zero), to a maximum of thirty six points.

Methods: Children aged ten years and over with IBD, and one parent, were recruited from the IBD outpatient clinic in Christchurch Hospital, New Zealand. Children completed IBD-STAR prior to their appointment. Parents and clinicians rated the child's SM skills using a series of five visual analogue scales (VAS) to correspond with each IBD-STAR section and one overall rating. Children and parents also completed qualitative questions to cross-validate IBD-STAR responses.

Results: Twenty five children participated, mean age 14 years (SD 1.7, range 10.8 to 16.9). Fourteen (56%) were male, 21 (84%) had Crohn's Disease. Data were collected on time since diagnosis, age at diagnosis, and parent education level. The mean IBD-STAR total score was 27.1 (SD 5.7), equivalent to a score of 75%. The mean score was significantly associated with increasing age ($p = 0.017$), but no other variable. When children's IBD-STAR scores were compared with parents' VAS scores, parents scored all sections lower, thus underestimating their child's reported skills. These differences were statistically significant ($p < 0.05$) for two sections (appointments, adherence) and overall. When IBD-STAR scores were compared with clinicians' VAS they were significantly different for one section (appointments) but not overall. The cross-validation questions were in agreement with IBD-STAR items for 85% of children's responses and 78% of parents. Reliability (measured using Cronbach's alpha) for the tool overall was high at 0.84 (section range 0.4 to 0.85).

Conclusion: IBD-STAR can produce SM skills reports from children that are closely aligned with the assessment of their clinician, but were underestimated by their parents - a common finding in the literature. Cross-validation techniques established that children reported their skills accurately, thus reducing the chance of IBD-STAR being subject to social desirability bias. Further testing is required in a larger, diverse population sample to establish generalisability. IBD-STAR may help identify children at risk of sub-optimal health autonomy who could benefit from additional support. Further research could assess whether IBD-STAR could be utilised for evaluating the efficacy of targeted SM interventions.

P-098

Latent tuberculosis testing in paediatric patients with inflammatory bowel disease treated with anti-tumour necrosis factor agents: do we need new testing recommendations?

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Introduction: Anti-tumour necrosis factor (anti-TNF) agents are one of the therapeutic cornerstones in inflammatory bowel disease (IBD). These agents increase the risk of reactivation of latent infections. Latent tuberculosis (LT) testing is recommended prior to anti-TNF therapy in paediatric patients with IBD. In the European Union, Portugal is one of the countries with the highest prevalence of tuberculosis, and the country's northern region has the third highest national notification rate registered in 2017: 20,6 cases per 100.000 inhabitants. Our department is Portugal's northern region paediatric gastroenterology reference centre.

Objectives and Study: This study aimed to evaluate the prevalence of LT and active tuberculosis in this group of patients.

Methods: We performed a retrospective and descriptive analysis of paediatric patients with IBD eligible for anti-TNF therapy followed at our department during the last 2 years.

Results: Clinical data from 273 paediatric patients with IBD was analysed. 120 of these patients were eligible for anti-TNF therapy (77,5% Crohn's disease, 21,7% Ulcerative Colitis, 0,8% IBD unclassified). The median age was 13 years. LT prevalence was 7,3% (n=9): positive Tuberculin skin test (TST) in 5 cases and positive Interferon-gamma release arrays (IGRA) in 4. In 2 cases initial IGRA testing was negative. A single patient had contact with a case of active tuberculosis. All patients diagnosed with LT were treated with isoniazid. Follow up after treatment of LT varied between 28 and 1496 days. We had no cases of complications or development of active tuberculosis.

Conclusions: Testing for LT prior to anti-TNF therapy is mandatory. Repeating this testing process while under anti-TNF therapy is dependent on a case-by-case analysis. Even in the absence of contact with active tuberculosis its important to test and treat LT. We believe that further studies are needed to formulate new recommendations for LT testing / testing repetition.

P-099

Physical activity and sedentary time in adolescents with inflammatory bowel disease: prevalence and risk factors

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Objectives and Study: The importance of physical activity in the prevention of chronic inflammatory diseases has been well established. It has been shown that higher physical activity levels (PAL) were associated with reductions in inflammatory serum markers. Thus, physical activity might be a protective factor against occurrence and progression of inflammatory bowel diseases (IBD). Yet, children with IBD tend to be less active than their healthy peers. The Canadian 24-Hour Movement Guidelines for Children and Youth recommend an average daily moderate-to-vigorous physical activity (MVPA) of at least 60 minutes 7 days a week.

The primary aim was to evaluate the prevalence of MVPA in Canadian adolescents with IBD as compared to their healthy Canadian peers. The secondary aims were to assess the clinical factors that might influence their PAL.

Methods: From June 2018, children with IBD, age ≥ 12 years, were prospectively surveyed during outpatient visits. PAL was assessed using the Canadian Health Measure Survey Children-Physical Activity Questionnaire. The responses were converted into metabolic equivalents of tasks (METs) by using validated tables. Clinical factors were compared between adolescents who reached the MVPA target and those who did not.

Results: We included 138 patients (79 males; mean (SD) age 15.5(1.6) years, 95 (68.8%) diagnosed with Crohn's disease and 32 (23.2%) with ulcerative colitis). Overall, 74.4% were in remission according to the Pediatric Crohn Disease Activity Index or Pediatric Ulcerative Colitis Activity Index (score ≤ 10). Yet, only 30.6% reached the Canadian physical activity target, as compared to 35.0% among their healthy peers. The median (IQR) duration of MVPA per day was 34.0 min (14.0 to 66.0) and of sedentarity was 5.7 hours (3.0 to 8.0). Although 45.7% of the patients claimed that they had discussed the significance of MVPA with their teachers or doctors, only 12% were aware of the national target. None of the following clinical factors showed significant association with the PAL: disease phenotype and activity, abdominal pain, anemia, arthralgia, arthritis and age.

Conclusions: Our study showed a low prevalence of MVPA in Canadian children with IBD. The recommended target among this population is far from being achieved. Likely explanations might be the excessive screen time of adolescents. No association between clinical or familiar factors and PAL was found. Thus, further physical activity recommendations from health providers are needed to help enhance PAL in all children diagnosed with IBD regardless of disease activity.

P-100

An audit of adherence to the New Zealand guideline for the assessment and diagnosis of paediatric inflammatory bowel disease at two New Zealand centres

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Objectives and Study: New Zealand (NZ) guidelines for the approach to diagnosis and management of inflammatory bowel disease (IBD) in children were developed in 2014. Adherence to these recommendations has not been established. The aim of this study was to audit the investigations and assessments obtained in children at the time of their diagnosis with IBD in NZ to establish consistency with the recommendations provided in the national guideline.

Methods: This retrospective, observational study, audited the recommended investigations as outlined in the 2014 NZ guidelines, in the most recent 100 children aged < 16 years diagnosed with IBD at Starship Child Health and Christchurch Hospital, New Zealand (the two tertiary paediatric gastroenterology centres in NZ).

Results: Fifty children diagnosed with IBD from 2017-2019 at each centre were included, with a median age of 11 years. Of the 100 children, 72 were classified as Crohn's Disease (CD), 15 as ulcerative colitis (UC) and 13 as IBD-unclassified. All 100 children underwent upper gastrointestinal (GI) endoscopy and colonoscopy with biopsies at diagnosis. Small bowel imaging was undertaken in 90% of children. Of children with CD, disease location was ileal in 13, colonic in 27, and ileocolonic in 32. Twelve of the 15 children with UC had pancolonic disease. Disease activity scores were available for all children at diagnosis. The mean PCDAI score was 55 in those with CD and the mean PUCAI score was 42 in the children with UC. All children had growth parameters and liver chemistry recorded at diagnosis. Most children (>90%) had albumin, erythrocyte sedimentation rate, varicella serology, thiopurine methyltransferase (TPMT) activity, faecal calprotectin and faecal microbiology performed. Vitamin D levels were measured in 72 children: 23% (14/62) children with CD and 30% (3/10) with UC were vitamin D deficient (25-OH vitamin D < 50 nmol/L) at diagnosis. Many children (70-89%) had iron studies, folate, vitamin B12 and creatinine levels obtained. Calcium and urea levels were both measured in 63% of children. Only 36% of children had serum magnesium, 37% serum phosphate and 12% serum zinc levels obtained at diagnosis. Very few children had Tanner stage or parental heights recorded. Records of historical growth data, family history of IBD and risk factors for tuberculosis were also variably recorded.

Conclusion: CD is the most frequent type of IBD in NZ children. The most recent 100 children diagnosed with IBD at NZ's two tertiary centres all underwent upper and lower GI endoscopy and the majority had small bowel imaging. Disease activity scores were obtained in all children. Although most children received recommended investigations at diagnosis of IBD, serum zinc, phosphate and magnesium levels were infrequently obtained.

Disclosure of Interest: ASD - Advisory Board membership for AbbVie, Janssen, Sanofi

P-101

Prevalence, management and outcome of mycobacterium tuberculosis infections in paediatric patients with inflammatory bowel disease in Singapore

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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 2008-2019 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 was performed at the time of IBD diagnosis prior to 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 11 patients out of a total of 200 IBD patients (prevalence 5.5%), 9 patients had Crohn's disease, 2 had ulcerative colitis. Anti-TNF therapy was used in 4 patients. Median age at diagnosis of IBD was 11 years (range: 1-17). TB was diagnosed based on IGRA (n=6), IGRA and TST (n=1), TST (n=1) and clinical/histopathologic findings (n=3). Eight patients had latent TB, of whom 6 were detected prior to starting any immunosuppressive treatment, 1 was detected 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) who had negative TB screening before 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 isoniazid/pyrazinamide combination therapy for 6-9 months (n=3), while 1 patient received isoniazid/rifampicin/pyrazinamide. 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 started/restarted after a median interval of 2.5 months (range: 0.01-28) from initiation of TB treatment. After a median follow-up duration of 6 years (range: 0.1-11), none of the 11 patients had active or reactivated TB infection, or serious adverse events with anti-TB medication. At last follow-up, all 11 patients had not achieved remission of their IBD; median faecal calprotectin level was 887µg/g (range: 276-1000).

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

Serum zinc and selenium status in paediatric patients with Inflammatory bowel disease: a retrospective multicenter study in Japan

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Objectives and Study: Zinc and selenium deficiencies in patients with inflammatory bowel disease (IBD) have been reported mostly from Western countries. Whether Japanese children with IBD have zinc and selenium deficiencies remains unclear. We aimed to clarify the prevalence of zinc and selenium deficiencies in Japanese children with IBD.

Methods: Subjects were retrospectively enrolled children under 17-year-old who visited at 12 paediatric centers in Japan between November, 2016 and February, 2018 and were divided into 3 groups such as children with ulcerative colitis (UC), Crohn's disease (CD), and normal control (NC) including patients with irritable bowel syndrome and healthy children. Serum zinc and selenium were measured by atomic absorption spectrophotometry. Zinc and selenium deficiencies were defined as < 70 µg/dL and < 9.5 µg/dL, respectively. We excluded patients who were treated with zinc and/or selenium preparations.

Results: Two hundred and fifty-nine subjects from 118 patients with UC (median age, 11 years), 98 CD (11y), and 43 NC (11y) were examined. Serum zinc and selenium levels were significantly lower in CD (median, 64 µg/dL and 12.6 µg/dL) than in UC (69 and 14.6; $P < 0.05$ and $P < 0.001$) and NC (77 and 15.7; $P < 0.01$ and $P < 0.001$), respectively. The prevalence of zinc deficiency was significantly higher in CD (60.2%) than in NC (37.2%; $P < 0.05$), but not in UC (51.7%; $P = 0.22$). The prevalence of selenium deficiency was significantly higher in CD (15.3%) than in UC (5.9%; $P < 0.05$) and NC (0%; $P < 0.01$).

Conclusions: Zinc deficiency is common in Japanese children with IBD. Serum zinc and selenium levels were significantly lower in Japanese children with CD than in UC and NC. Our study supports the role for monitoring and replacement of zinc and selenium in children with IBD, particularly with CD.

Disclosure of Interest: This study was supported by Nobelpharma Co., Ltd.

P-103 (Poster of Distinction)

Time-to-reach target calprotectin level and relation with first relapse in newly diagnosed patients with IBD: first results of the Fast Forward Care Prospective Registry

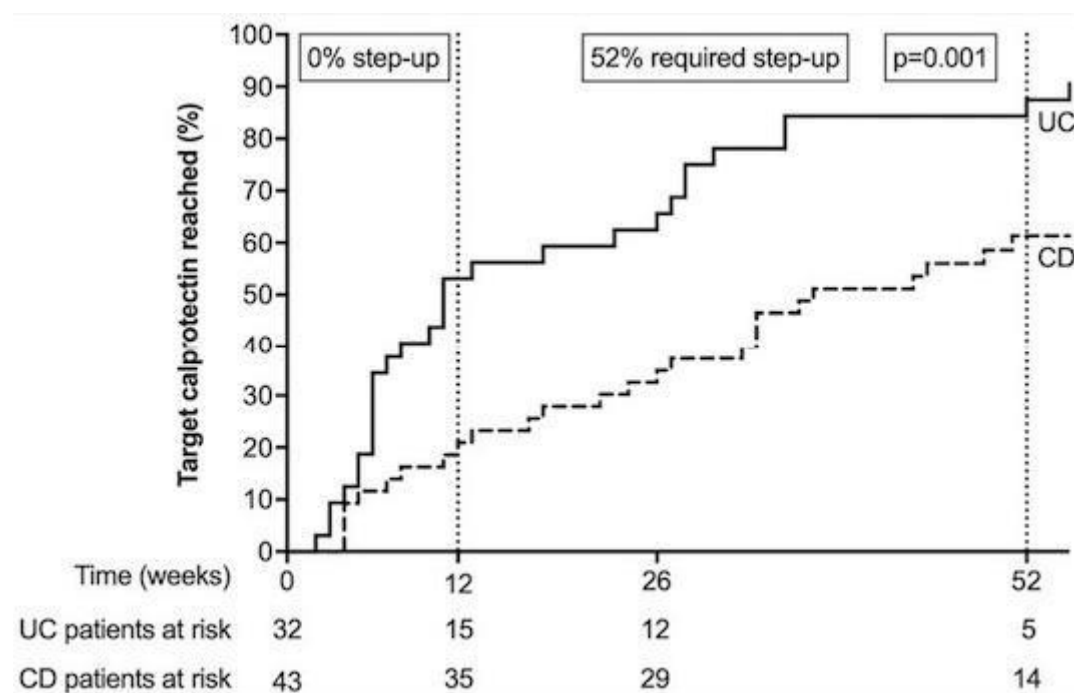
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Objectives and Study: Treatment targets in IBD move away from controlling symptoms towards complete recovery of the intestinal mucosa. Currently, the most frequently used noninvasive surrogate marker of mucosal healing is a faecal calprotectin concentration in the target range. This study tested if there was a relation between time-to-reach target calprotectin and first relapse.

Methods: We prospectively included new-onset IBD patients aged 17 and younger in a cloud-based registry (FastForwardCare) and followed them for at least 52 weeks. They were treated according to Dutch national guidelines that advocate a step-up approach. Time-to-reach target was defined as the first calprotectin measurement below 250 µg/g after the start of induction therapy. Time-to-first relapse was defined as the time from the first calprotectin measurement below 250 µg/g until reintroduction of induction therapy.

Results: We included 76 patients (luminal Crohn's disease (CD) 43); ulcerative colitis (UC) 33). Median age at diagnosis was respectively 14.5 and 14.1 years. The figure shows that the median time-to-reach target calprotectin was 37 weeks in CD and 11 weeks in UC patients (Log-rank test, $p=0.001$). Once the calprotectin target was reached, remission lasted significantly longer in CD than in UC patients (Log-rank test, $p=0.001$). Reaching the target within 12 weeks is associated with long-lasting remission in CD, but not in UC (Log-rank test, $p=0.057$).



[Figure. Kaplan-Meier plot demonstrating time-to-reach target calprotectin (< 250 µg/g)]

Conclusion: The findings of this prospective registry suggest that a quick response to conservative induction therapy predicts long-lasting remission in new-onset paediatric CD, but not in UC. Prospective registries, such as FastForwardCare, are well suited for studying treatment effectiveness in real-world practice.

Residence in rural jurisdictions with reduced medical accessibility is associated with more corticosteroid treatment for Israeli children with Inflammatory Bowel Disease

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Objectives and Study: We hypothesized that social economic status (SES) and living in rural areas remote from medical centers are associated with higher corticosteroids use, as proxy markers of poorer disease control in pediatric Inflammatory Bowel Disease (IBD).

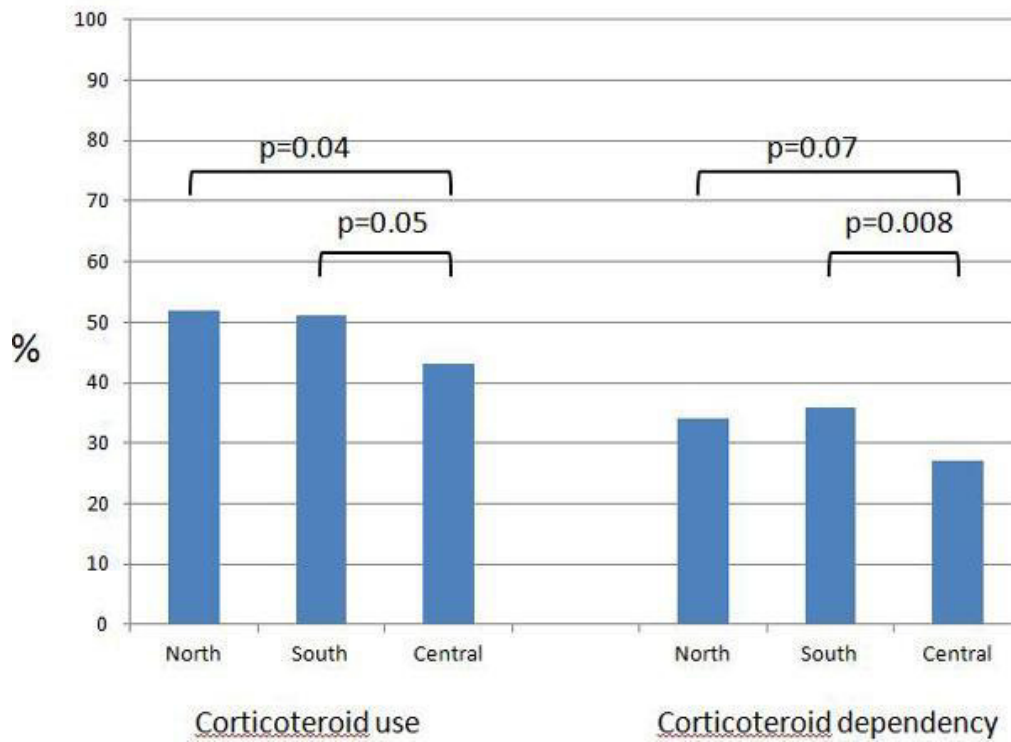
Methods: Children with IBD (< 18 years old) from 3 out of the 4 national health maintenance organizations (HMOs) covering 48% of the Israeli population, were identified from the validated epiIIRN database in which all IBD cases in Israel are identified from the HMO's contacts with sensitivity and specificity of 89% and 99%, respectively. Medication use is highly accurate in the database given the national coverage of its cost. SES scale (1-7 low, 8-12 middle, >13 high) and geographical districts (central, northern and southern) were assigned to all patients.

Results: 2,956 children identified between 2006-2018: 1,978 (67%) with Crohn's disease (CD), 929 (31%) with ulcerative colitis (UC) and 49 (2%) general IBD code. 2,393 (81%) were from central districts and 563 (19%) from peripheral regions. Steroid use at any time during 2006-2018 among children with CD was significantly higher in the north and the south compared to central districts . Among children with UC the difference was apparent only in the south. (Figure 1) Steroid dependency at any point during 2006-2018 (defined as ≥ 3 corticosteroid purchases per year) among children with CD was also significantly higher in the North and the South than in central districts. No difference was apparent among children with UC. (Figure 1) SES did not impact corticosteroid usage, whether in a univariable or multivariable model.

Conclusion: There was higher usage of corticosteroids, and higher corticosteroid dependency in peripheral regions than in central districts in IBD, possibly suggesting less tight disease control. When comparing steroid usage per SES, no significant differences were found.

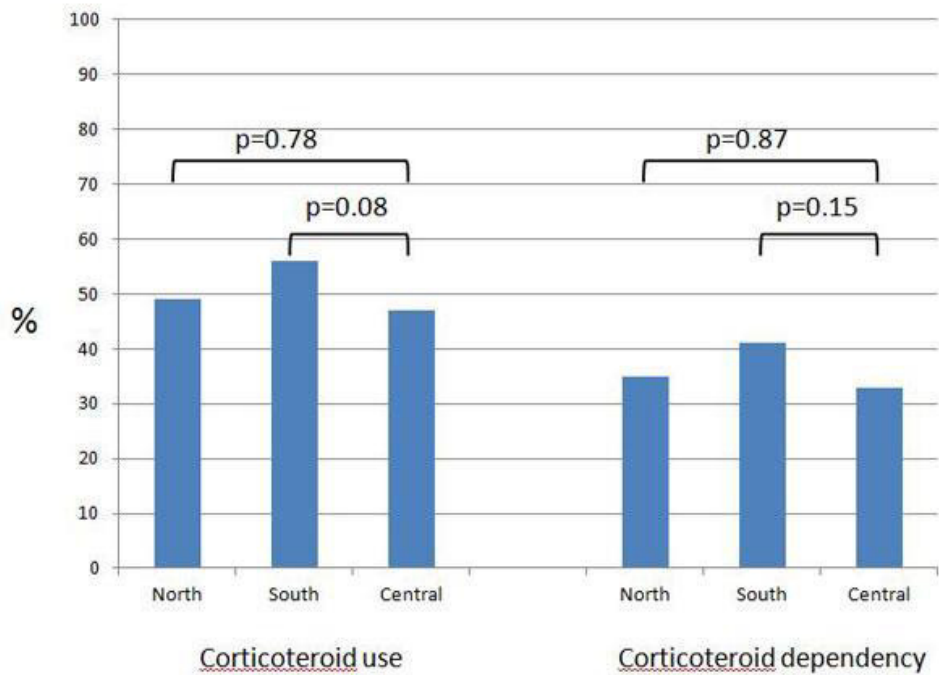
Supported by a grant from the Leona M. and Harry B. Helmsley Charitable Trust

Crohn's Disease



[Crohn's Disease]

Ulcerative colitis



[Ulcerative colitis]

Health-related quality of life impact of steroids versus exclusive enteral nutrition for induction in a large Canadian pediatric IBD inception cohort

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Objectives and Study: Assessment of health-related quality of life (HRQOL) is key in pediatric Crohn's disease (CD). IMPACT is a disease-specific HRQOL self-report tool, while PedsQL is a generic HRQOL tool completed by children and/or their parents. Study objective was to assess whether type of induction therapy for CD had an effect on HRQOL as measured by IMPACT or PedsQL at 0 months, 6 months and 12 months.

Methods: Data was obtained from the Canadian Children IBD Network inception cohort study, which is a multi-centre, prospective study of children ≤ 17 years with IBD. Data was extracted for patients with CD ≥ 8 years who received steroids or exclusive enteral nutrition (EEN) as induction therapy. IMPACT and PedsQL are reported as both total and domain scores. Scores range from 0-100, with a higher scores indicating better HRQOL. Time points were established in defined 'semesters': ranges of dates on either end of 0, 6 and 12 months. Differences were compared between groups using independent samples t-tests, Mann-Whitney U tests or chi-square tests.

Results: 547 participants with CD completed IMPACT and/or PedsQL. At baseline, those starting steroids had higher disease activity as measured by wPCDAI ($p = .002$). At 6 months, there was no difference in wPCDAI between the two groups. There was no statistically significant difference in physician global assessment of disease activity between groups at any time point ($p = .065$ at 0 months, $p = .514$ at 6 months, $p = .779$ at 12 months). There were no differences in number of hospitalizations or surgeries within 3 months of IMPACT completion between groups. The EEN group had significantly higher mean IMPACT total scores 6 months post-induction therapy ($p = .001$), these differences were also seen for the emotional, social and well-being domain scores of IMPACT. The EEN group had significantly higher mean PedsQL total scores 12 months post-induction therapy ($p = .047$).

Conclusion: Pediatric patients receiving EEN as induction therapy for CD had significantly higher HRQOL scores 6 months post-induction as measured by IMPACT. Fewer significant differences were noted between groups as measured by PedsQL, a generic measure of HRQOL.



[Mean IMPACT and PedsQL total scores between treatment groups at baseline, 6 Mo, and 12 Mo]

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Knowledge of medication and adherence to medication in patients with pediatric inflammatory disease

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Objectives and Study: Inflammatory bowel disease is a chronic disease, including Crohn's disease and ulcerative colitis. It is a lifelong disease that occurs in about 20% of teenagers. There are studies that patients with chronic diseases have more disease related complications with more knowledge about their diseases. In addition, low medication adherence to adolescents in patients diagnosed with IBD in childhood and adolescence is an important factor promoting the deterioration of disease. The purpose of this study was to investigate the knowledge of medicine and adherence to medication of patients diagnosed with IBD in children and adolescents.

Methods: We reviewed the medical records of patients who were diagnosed with IBD in children and adolescents and who were followed up at our institute. Diagnosis, location, behavior, medications, surgical outcome, and number of endoscopies were retrospectively reviewed. Patients taking more than 80% of the medicines prescribed over the past week were defined as those with "high adherence to medication".

Results: Of 93 patients, 59 (63.4%) were men and 78 (83.9%) were Crohn's disease. Mean age at diagnosis was 13.8 ± 2.8 years, mean duration of disease was 57.8 ± 41.1 months, mean age was 18.6 ± 3.7 years, and 34 patients (36.6%) were over 20 years of age. Sixty-five patients (69.9%) knew exactly the name of the oral medication currently in use and 34 patients (36.6%) knew the exact amount. Only 15 patients (16.1%) knew the medicines they used in the past. Among the 55 patients using the injection, 33 patients (66.0%) correctly knew the name of the medicine. 72 patients (77.4%) answered that they did not know the side effects of the medicines they were using. Sixty-four patients (66.8%) received more than 80% of prescribed oral medicines one week before arrival. ($P = 0.028$). The more knowledge about past medications ($p = 0.008$), the more knowledge about medicine related adverse effects ($p = 0.020$), the higher the adherence to medication. Diagnosis did not show association with adherence to medication with statistical significance, but 40% of patients with ulcerative colitis had low adherence to medication.

Conclusions: Many children and adolescents suffering from IBD had a low adherence to medication. Only 66.8% of patients took more than 80% of the medicines. Adherence to medication was low in the older aged group and in the group with high knowledge of the medicine. As specialists in charge of treat pediatric IBD, we should strengthen educating not only disease itself but also importance of adherence to medication, which may promote the adherence to medication and control their diseases.

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Health-related quality of life in Brazilian adolescents and young adults (AYA) with inflammatory bowel disease

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Objectives and Study: To assess the HRQoL in AYA IBD patients and compare to healthy controls. After we evaluate HRQoL between CD (Crohn’s disease) AYA and UC (ulcerative colitis) AYA population and analyze the influence of disease active status, extra-intestinal and treatment on HRQoL.

IBD essentially comprises Crohn’s disease (CD) and ulcerative colitis (UC), both are characterized by unpredictable exacerbations and remissions. The incidence is highest in adolescence and early adulthood and alike other chronic disease have a considerable impact upon patients' HRQoL. Few studies assessing HRQoL have been performed in AYA populations.

Methods: 59 AYA IBD patients (13-25y) at two gastroenterology units of tertiary hospitals was evaluated and compared to 60 AYA healthy controls (13-25y). All participants and the adolescents' legal guardian written informed consent form. Generic PedsQL4.0 version questionnaire for AYA and SF-36 only for adults were applied. After we compared only CD AYA vs. UC AYA population and consider the diseases’ factors that could influence the HRQoL.

Results: The PedsQL4.0 domain "school/ work" and SF-36 domain "general health perception" was reduced in IBD patients compared with healthy controls group. "Health change" domain of SF-36 was lower in UC AYA patients compared to CD. No significant difference among extra intestinal manifestation and disease activity was observed between both groups. Autoimmune sclerosing cholangitis was diagnosed only in UC AYA patients. Use of prednisone was significantly higher among UC patients and previous gut surgery was significantly higher between CD AYA patients.

Conclusions: HRQoL was significant lower for AYA with IBD relative to healthy controls. This results highlight areas to focus clinical attention in adolescents and young adults patients with IBD for assessment and future interventions.

	IBD patients (n=59)	Healthy controls (n=60)	p
age, yrs	18 (13-25)	20 (13-25)	0.598
BMI, kg/m ²	20 (14-30)	21 (15-28)	0.659
School years	11 (8-17)	15 (6-15)	0.072
Upper /middle socio-economic classes	33/35	39/40	0.596
PedsQL™4.0			
School/Work	70 (10-100)	75 (0-100)	0.037
SF-36			
General health perceptions	50 (10-80)	70 (25-90)	0.0002
Pain VAS scale	2.0 (0-10)	1.0 (0-7)	0.111

[Demographic datas, PedsQL 4.0 and SF-36 scores of AYA IBD patients and Healthy controls]

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The impact of inflammatory bowel disease on the psychosocial functioning of children and teenagers in New Zealand

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Objectives: New Zealand (NZ) has one of the highest rates of IBD in the world, with increasing incidence noted in children in NZ over recent years. IBD has the potential to affect many areas of functioning. Health-related quality of life (HRQoL) is an outcome measure that attempts to take into account the lived experience of the individual, and is becoming increasingly relevant to current research and understanding of the impact of IBD on individual functioning. Research regarding this topic is limited at best, particularly among children with IBD. To date, only one published study has investigated the impact of IBD on the HRQoL of children and adolescents in NZ. The current study aimed to further investigate the HRQoL of children and adolescents in NZ and to understand what factors might affect overall HRQoL. It was hypothesised that the IMPACT-III measure of HRQoL would exhibit good to excellent reliability scores, that duration of disease would predict HRQoL and that disease severity would predict HRQoL overall and subscales of the IMPACT-III tool.

Methods: Children aged 18 years or less, resident in the South Island of New Zealand with diagnosis of IBD (CD, UC, or IBDU) were recruited prospectively. After completing informed consent, participants aged between 9 and 18 years of age were asked to complete IMPACT-III questionnaires. Clinical data, disease activity and other relevant data were also collected. Physicians Global Assessment (PGA), Pediatric Crohn disease activity index (PCDAI) and Paediatric ulcerative colitis activity index (PUCAI) scores were derived.

Results: Ninety-one children completed baseline IMPACT-III questionnaires. Fifty-six were male, 89 European, 79 were diagnosed with CD and mean age was 13.4 years. Internal reliability of the IMPACT-III scores were reflected in Cronbach α scores of 0.93 for the total score, with scores that varied from acceptable to good for the sub-scales. There was no relationship between duration of disease or subject age and their IMPACT-III scores. Disease severity (assessed as PGA, PCDAI or PUCAI) was correlated with IMPACT-III scores ($P < 0.05$ for all). Furthermore, disease severity correlated with subscales, in particular, the social functioning subscale.

Conclusions: These findings in a population of NZ children provide further evidence that disease severity is a significant influence on the HRQoL of children with IBD, highlighting the importance of optimal management to reduce the detrimental impact of active disease on HRQoL. These results suggest that assessment of HRQoL could be considered as a clinical tool to identify those individuals who are at greatest risk for poor developmental and HRQoL outcomes.

Evaluation of a screening process for the psychological wellbeing in a paediatric inflammatory bowel disease (PIBD) clinical population - a 4-week pilot study

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Objectives and Study: We aimed to assess a screening process for psychological well-being in a PIBD population over a period of 4 weeks, in order to improve our quality of care and to evaluate how to best routinely capture any psychological needs at medical outpatient appointments. We focused on exploring the nature of the psychological need, whether the measures selected capture the general wellbeing of this population as hoped and the efficiency of the screening process.

Methods: Patients and their carers who attended consecutive outpatient appointment (OPA) were asked to complete the *Paediatric Quality of life Inventory* (PedsQL, Varni et al. 2004) and the *Revised Children's Anxiety and Depression Scale* (RCADS, Chorpita et al. 2005) whilst waiting to be seen by their physician. We also explored any current or previous access to psychological input by asking carers and patients and consulting hospital records. The collected information was examined and implications for the need of this group were explored. This pilot was a convenience sample of small size.

Results: Over a period of 4 weeks, 14 patients consented participation, however only 9 participants completed all questionnaires (age range 3 to 15 years, 5 males). Results on the PedsQL showed lower mean scores than reported in the UK general population means, with a significant impact on the quality of life for 5/9 (55.5%) of the patients. On the RCADS, 5/5 (100%) carers and 3/5 (60%) children showed total scores related to elevated levels of depression and anxiety. However, 60% of patients presented with additional complexities (Autistic Spectrum Disorder, learning disability, complex medical diagnoses) which would demonstrate that it is difficult to interpret the meaning of significant scores. These scores may well not relate to the presence of PIBD and the norms for the RCADS measure are not valid in these complex presentations.

Reasons for non-participating patients were lack of time and complaints about the lengthy forms. Psychology access was already available in 66.6% (6/9), 55.5% (5/9) at our centre and 11% (1/9) locally. The patients who presented with additional comorbidities 33.3% (3/9) were not accessing psychological support tailored to their needs and were referred accordingly.

Conclusions: This pilot study showed that the nature of the psychological need for psychology input is not always related to the presence of PIBD requiring specialised paediatric health psychology. The screening process showed that both measures equally captured emotional needs of patients. Therefore a single routine screening tool (PedsQL), accompanied by a triage tick box questionnaire prior to the OPA, could be used to detect comorbidities and identify appropriate services needed

P-110 (Poster of Distinction)

Transition test is a valid tool to monitor disease knowledge in adolescents with IBD transitioning to adult care

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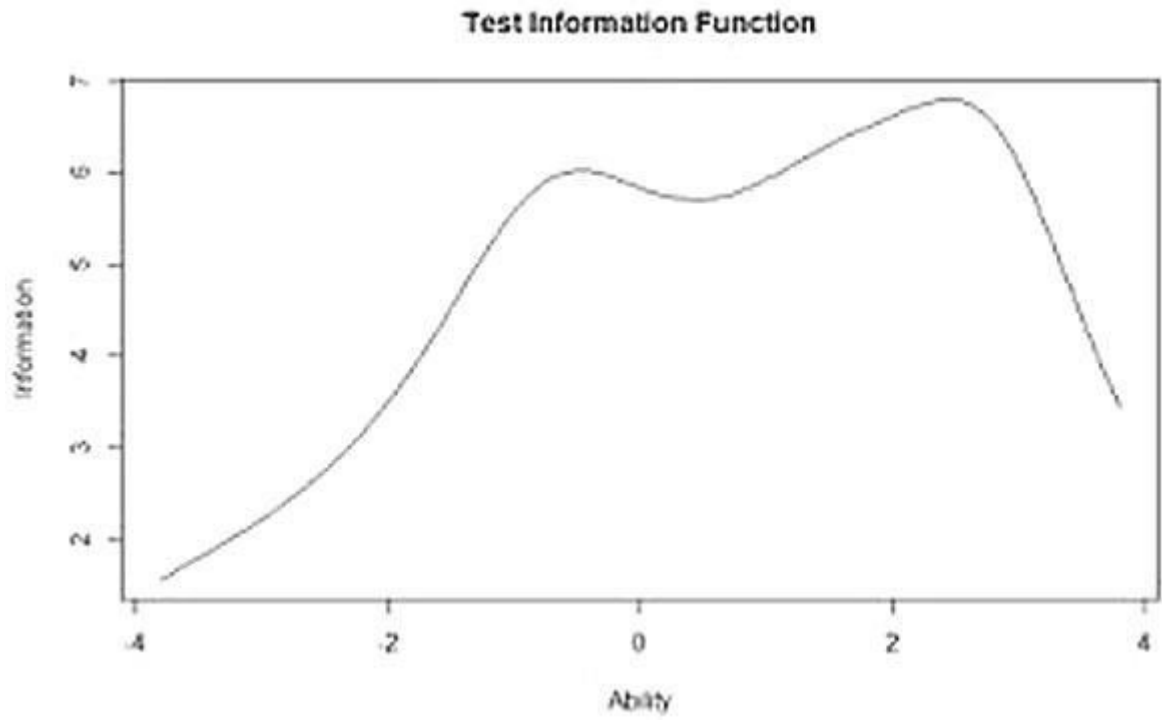
Objectives and Study: Transition of adolescent IBD patients to adult health care is often troublesome. Transitional programs are designed to result in successful transfer around the age of 18 years. Knowledge about IBD is thought to be important in the process of transition. We developed an IBD-specific knowledge questionnaire, the Transition Test (TT) and aimed to validate this test in this study.

Methods: This prospective validation study was performed in 2016-2018 in all consecutive patients (aged 16-18) visiting the transition clinic. The TT has 25 open questions about IBD, medication, life with IBD, and transition. Patients were asked to do the TT during maximal 4 occasions: at age 16, 17, at the last transition clinic visit (around 18) and 1 year after transfer to adult care. A correction model was developed and inter-rater agreement was assessed by Cohen's kappa coefficient. Using a Rasch model we determined the difficulty of the questions and how well they distinguished between patients. Cronbach's alpha was used to demonstrate reliability. Patient factors (age, disease, educational level, medication use, illness acceptance and independence from parents) were correlated to total score of the TT.

Results: A total of 207 TTs were evaluated in 111 patients (63.1% male, 58.6% CD, 36% UC, 5.4% IBDU). After 5 rounds of assessments by 3 investigators, and revision of the correction model, a kappa score of > 0.61 (0.61-0.88) was achieved for all 25 questions. Reliability with Cronbach alpha was good (0.856).

The TT discriminated well between the different levels of knowledge (from -2 to 4 SDS), between low (-2SDS) and high (2SDS) levels of knowledge better than between low (-2SDS) and very low scores (-4SDS) (Figure). Knowledge increased in patients who did repeated TTs, especially in patients having lower TT scores at first TT. Questions about smoking, alcohol, drugs and heredity yielded little information between levels of knowledge. Male gender, low educational level, disease acceptance problems and dependence on parents were factors associated with a significantly lower total TT score. Prednisone use in the prior 3 months and treatment with a biological was associated with significantly higher TT scores. Disease activity was not a significant factor.

Conclusion: The Transition Test (TT) is a reliable and valid questionnaire, with a good correction model. This specific IBD-knowledge questionnaire can be used at the transition clinic to detect gaps in knowledge in adolescents with IBD. Results of the TT can guide the transition team as to what issues to discuss with the adolescent IBD patients. The TT can be used to assess changes in knowledge over time. The TT is a valid tool to single out patients with low scores (but does not discriminate from patients with very low knowledge). As is often seen with questionnaires, girls and patients with higher education level scored higher on average. Adolescents using steroids and/or biologicals had significantly higher TT scores, suggesting a higher level of concern in these patients.



[Test information function]

P-111

Lupus enteritis, an uncommon initial presentation of systemic lupus erythematosus: a case series

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Introduction: Lupus enteritis (LE) is a rare and atypical initial presentation of systemic lupus erythematosus (SLE). We illustrated three children presenting initially with predominantly gastrointestinal (GI) symptoms mimicking inflammatory bowel disease without the typical SLE symptomatology who were subsequently diagnosed to have lupus enteritis.

Case 1: An 8-year old girl presented with a four-month history of intermittent abdominal pain associated with vomiting, diarrhoea and weight loss of 8 kg. There was a history of non-specific skin rashes and joint pains. Upper endoscopy and colonoscopy were unremarkable. Capsule endoscopy showed small bowel erosions. She was initially treated as small bowel Crohn's disease and was started on exclusive enteral nutrition but did not show any improvement. Further investigations revealed positive antinuclear antibody (ANA; 1:320), positive anti-dsDNA antibody and anti-RO antibody, low complements and proteinuria. CT scan showed diffuse thickened small bowel wall with ascites. She was diagnosed to have LE and started on intravenous corticosteroid.

Case 2: A 10- year old girl presented initially with 1 month's history of poor appetite followed by recurrent episodes of severe vomiting over the following 3 months, associated with progressive weight loss of 8 kg. She subsequently also developed intermittent epigastric pain and watery diarrhoea. There was history of fatigue, intermittent right ankle pain, mild hair loss and transient malar rash. She had leucopenia, lymphopenia and normochromic normocytic anemia, hypoalbuminemia and mild proteinuria. She had a positive ANA 1:320 (homogenous pattern) , positive anti-dsDNA antibody, low complements and was positive for direct Coombs test, anti- thyroglobulin and anti- thyroperoxidase antibodies. She was diagnosed as LE and started on intravenous corticosteroids.

Case 3: An 11-year-old boy presented with history of chronic weight loss (about 30kg) over a year followed by a 6-week history of intermittent abdominal pain with vomiting and diarrhoea. He has no other symptoms of SLE. Bloods investigations showed anaemia, leukopenia, low complements, high ESR and positive ANA (1:1280) with proteinuria and microscopic haematuria. Stool calprotectin was negative. CT scan showed diffuse bowel thickening over small bowel and colon with target signs to suggest submucosal oedema. Endoscopy revealed an oedematous jejunum, terminal ileum and colon. He was diagnosed to have LE and started on intravenous corticosteroid.

Conclusion: It is important to recognise lupus enteritis in patient presenting with chronic diarrhoea and gastrointestinal symptoms as it is a serious potential life-threatening complication of SLE if not treated promptly.

P-112

Two patients with inflammatory bowel disease and glycogen storage disease type 1 - differences and similarities of type 1a and type 1b

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Objectives and Study: We report two patients with inflammatory bowel disease (IBD) and glycogen storage disease (GSD) type 1a and type 1b, respectively. GSD 1a is associated with immune deficiency with neutropenia and development of Crohn's like disease. For GSD 1b an association with IBD was not known until 2017.

Results:

Patient 1 is a 17 years old male with known GSD 1b. His family is from Turkish origin without parental consanguinity. In 2014 he developed chronic non-bloody diarrhoea and microscopic colitis was diagnosed. For three years his colitis was in remission under oral 5-ASA. In 2017 he had a flair with moderate pancolitis with ulceration and stenosis of the ileocecal valve and a deep ulcer 40 cm above the anus. Induction therapy with corticosteroids and maintenance therapy with azathioprine were initiated. Relevant side of the corticosteroid therapy in the form of severe blood sugar level fluctuations could be managed in cooperation with our Centre for Metabolic Diseases.

At the time of the flair repeated measurement showed low absolute neutrophil counts (ANC) under 500/ μ L and insufficient levels of 6-thioguanine nucleotide (6-TGN) due to poor adherence to granulocyte-colony stimulating factor (G-CSF) and azathioprine therapy. Because of persistent colonic inflammation in the course of the disease therapy was switched to Infliximab (IFX) as monotherapy which led to a maintained remission for one year until know.

Normalization of ANC by G-CSF therapy leads to a better control of IBD in patients with GSD 1b. Most important side effect is the risk of development of malignant haematological diseases such as acute myeloid leukaemia and myelodysplastic syndromes. For this reason, regular haematology tests are recommended.

Patient 2 is a 17 years old female with GSD 1a. Diagnosis of IBD with duodenitis, terminal ileitis with epithelioid granuloma and pancolitis was established at the age of 12 years. Induction of remission was successful using Adalimumab (ADA). Maintenance therapy consisted of ADA and azathioprine as combo-therapy. Because the patient developed anti-drug antibodies resulting in loss of clinical response a switch to IFX was performed. She is in remission under IFX for one year know. In contrast to GSD 1b, GSD 1a does not lead to neutropenia or dysfunction of neutrophils. However, also in GSD 1a patients a high prevalence of IBD up to 8% is reported. Pathogenesis of IBD development in GSD 1 is still unknown. One explanation could be that the underlying enzyme defects in GSD lead to intestinal abnormalities that can cause IBD. As another possible explanation, changes in the gut microbiome due to high doses of corn-starch as nutritional management of GSD are discussed. Furthermore, a genetic predisposition for both GSD and IBD in a certain population rather than a direct causative link between GSD and IBD is subject of discussion.

Conclusions: In the two patients reported here, escalation to anti-tumour necrosis factor therapy was necessary, effective and safe. In GSD 1b adequate therapy with G-CSF is an important therapeutic option.

P-113

Autologous hematopoietic stem cell transplantation in refractory Crohn's disease - case report

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Objectives and Study: A significant percentage of Crohn's disease (CD) patients suffer an aggressive disease course, refractory to available approved medical therapies. Increasing evidence supports Autologous Haematopoietic Stem Cell Transplantation (AHSCT) could be a therapeutic option

Methods: A 19y male CD patient with refractory CD were submitted to AHSCT. The CD diagnosis was since he was 11y and only when he was 18y he could sign the consent term for AHSCT. He had an inflammatory and colonic phenotype, he was negative for Xlinked inhibitor apoptosis protein (XIAP) and doesn't have previous surgery. He had failed to a median of 6 lines mono or combined therapies and before the AHSCT was corticoid dependent. The patients completed the mobilization, apheresis, conditioning and transplantation phases, during a time of hospitalization of 30 days. Our hospital postulate the use of CD34(+) selection with Miltenyi Biotec system to improve the results based on the memory cells decrease (2). Stem cells were mobilized from the peripheral blood using cyclophosphamide (2 g/m²) and GCSF (10 µg/kg/day), enriched ex vivo by CD34(+) selection, and reinfused after immune suppressive conditioning with cyclophosphamide (200 mg/kg) and (rabbit antithymocyte globulin ATG (5 mg/kg)

Results: During mobilization and after transplantation the patients had lifethreatening complications and severe infectious as KPC and reactivation of cytomegalovirus disease. He had febrile neutropenia, mucositis, anemia. After 2y follow up all six patients achieved the primary and secondary outcomes: clinical and endoscopic remission (Picture). He had osteoporosis and bilateral ocular cataract as an adverse effect of corticosteroids. Now he is on the second year of post AHSCT without any medication and .

Conclusions: We consider AHSCT may be a promising therapeutic option for treatment refractory CD patients. The high complexity, toxicity, risk of death and infections, more accurate protocols need to be discussed between GI and oncohematology professionals and center around the world.

Growth retardation as the 'only' presenting symptom of Crohn's disease - a case series

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Objectives and Study: To present a case series of three children and adolescents with Crohn's disease (CD), who presented 'solely' with flattening of their height charts and with short stature.

Methods: Demonstration of three clinical cases. In two cases, the patients were male and in one female. These children presented to an endocrinologist at ages 11, 13 and 15 respectively with a chief complaint of short stature and flattening of their height curves. All of them were diagnosed with CD of various extent and severity.

Results: Upon examination, all three patients showed flattening of their height charts preceding their first endocrinological examination by many years. Their annual growth rates were 2,1;3,2 and 3,5 cm respectively. Laboratory work-up showed changes suggestive of CD [elevation of erythrocyte sedimentation rate (average 22 mm/hour), elevation of C-reactive protein (average 30,2 mg/l) sideropenic anaemia (average haemoglobin 10,1 g/dl, average mean corpuscular volume 65,5 fl), hypalbuminaemia (average 34,9 g/l), thrombocytosis (average 576×10^9), positive anti-saccharomyces cerevisiae antibodies (ASCA) and marked elevation of faecal calprotectin (FC, above 1000 ug/g)]. Due to the absence of other clinical symptoms suggestive of CD, a scintigraphy of the gastrointestinal (GI) tract using ^{99m}Tc HMPAO (Technetium HexaMethylPropylenAmineOxime) labelled leukocytes was performed. Scintigraphy results showed pathologic accumulation of leukocytes in the ileocecal area in all cases. The colon was affected in varying degrees among these patients. These findings were further supportive of the suspicions of CD. A magnetic resonance enterography (MRe) was performed to evaluate small intestine affections. In two cases, MRe showed typical inflammatory changes in the terminal ileum and various portions of the jejunum. In one case, isolated oedema of the jejunum was found. Upper and lower endoscopies were completed, CD was confirmed on both macroscopic and microscopic levels. All three patients were diagnosed with CD affecting both the small and large intestine to various degrees.

To induce remission, all three patients were started on exclusive enteral nutrition (EEN). In one case, and due to clinical intolerance, EEN had to be replaced with steroids. For maintenance of remission, azathioprine was commenced. Because of the severity of the growth retardation, an accelerated step-up approach to biological treatment with adalimumab was performed. The combined therapy proved to be effective in all three patients and growth catch-up was documented.

Conclusions: This case series demonstrates that CD can present with clinically isolated growth failure in the absence of traditional GI symptoms (abdominal pain, nausea, vomiting, diarrhoea, weight loss), thus emphasizing the importance of exclusion of this illness in the case of flattening of the height charts and/or small stature even in the absence of GI complaints. Measurement of FC seems to be an effective, accessible and non-invasive method that should be used for screening in this group of children. Due to the low specificity of FC and in case of absence of GI symptoms, performing a scintigraphy of the GI tract seems to be a sensitive way to avoid performing needless endoscopies in the case of absence of pathological accumulation of leukocytes.

P-115

De novo Crohn's disease after ileal pouch-anal anastomosis: A report of two cases

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Objectives and Study: Crohn's disease (CD) of the pouch is a relatively new disease entity lacking a uniform definition and diagnostic criteria, with a reported frequency of 2.7-13% across the medical literature.

Methods: This report details the cases of two children who developed findings compatible with Crohn's disease after undergoing restorative proctocolectomy with ileal-pouch anal anastomosis (IPAA) for an original diagnosis of early-onset ulcerative colitis (UC).

Results: Two Caucasian children, aged 3 and 12, were followed at our Unit since the endoscopic and histological diagnosis of early-onset (2 and 3.4 years, respectively) UC (Paris E3). They underwent restorative proctocolectomy and IPAA for chronic active colitis after 10 and 27 months from diagnosis, after infliximab and azathioprine failures. The two patients presented with increased stool frequency, fecal urgency, incontinence, and abdominal pain 12 and 60 months after surgery, respectively. Pouch endoscopy with mucosal biopsy was performed, with the macroscopic evidence of ileum aphthoid erosions. Histologic evaluation showed crypt architecture irregularities (cryptitis), basal plasmocytosis and the presence of granulomas, suggesting a diagnosis of active CD. Pelvic magnetic resonance imaging showed no perianal involvement. At the start, patients were treated with the steroids combined with azathioprine. After steroid withdrawal, azathioprine was continued to maintain remission. At 6 (case 1) and 36 (case 2) months follow up, 3 to 4 bowel movements per day were reported, with no associated gastrointestinal symptoms.

Conclusion: De novo CD is an increasingly recognized diagnosis after IPAA. Diagnosing de novo CD of the pouch is challenging, especially because symptoms mimic other inflammatory and noninflammatory bowel disorders, such as pouchitis, "cuffitis", and irritable pouch syndrome. Pouch endoscopy with biopsy should be the initial step in diagnosis.

P-116

Long-term maintenance of remission without treatment in an infant with ulcerative colitis after chemotherapy for colonic lymphoma associated with ulcerative colitis

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A girl aged 2 years and 7 months was diagnosed with total ulcerative colitis following colonoscopy at another hospital, and after suffering from abdominal pain and bloody diarrhea since the age of 1 year 9 months. She started mesalazine (5-ASA) and elemental diet treatment, but underwent repeated relapses requiring multi-drug therapy involving prednisolone (2 years 8 months to 3 years 3 months), azathioprine (2 years 11 months, 2mg/kg/day), and tacrolimus (3 years 4 months); repeat colonoscopy was performed every year. At the age of 5 years 7 months, colonoscopy showed slight erythema and four elevated lesions 2-5 cm diameter involving the descending and sigmoid colon. Biopsies of these lesions revealed a diffuse proliferation of large heteromorphic lymphocytes with the following immunohistochemical pattern: CD3⁻, CD10⁺, CD20⁺, BCL2⁻, BCL6⁺, and MUM1/IRF4⁺. The histological diagnosis was diffuse large B-cell lymphoma and the patient was then assessed at our hospital. An Epstein Barr Virus infection test was negative. Head, thoracic, abdominal, and pelvic computed tomography scanning revealed that the tumor was limited to the descending and sigmoid colon with no metastasis. A bone marrow aspirate showed no abnormal cells. The patient was diagnosed with stage II cancer according to international classification criteria (Murphy classification).

She was first started on dexamethasone, methotrexate, vincristine, cyclophosphamide, pirarubicin, cytarabine, and etoposide chemotherapy (B-NHL03 regimen). After chemotherapy, colonoscopy showed that elevated lesions in the descending and sigmoid colon had disappeared. Furthermore, mucosal healing was observed in the colonic mucosa from the rectum to the cecum.

Her family did not wish her to undergo surgery or receive biological therapy for UC. Additionally, she had shown intolerance to 5-ASA, tacrolimus had decreased renal function, and azathioprine may have caused malignant lymphoma development. Therefore, we decided not to treat her further. She continued remission for 4 years with no treatment for UC. Constant monitoring with colonoscopy (every 4-6 months) during follow-up showed no recurrence of malignancy or relapse of UC.

P-117

Use of ustekinumab in an infant with very early onset inflammatory bowel disease: 9 months follow-up

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Treatment in very early onset inflammatory bowel disease (VEOIBD) is challenging when no genetic defect is found. We describe the successful use of ustekinumab in an infant with VEOIBD. The healthy born infant developed bloody diarrhea at the age of 5 months. Since both parents were allergic, a cow's milk protein allergy was suspected. An extensive protein hydrolysate was started with temporary improvement. At relapse, a left colonoscopy showed follicular hyperplasia with histologic signs of allergic colitis at 8 months of age. A diet without cow's milk, eggs and soy but with an elemental formula resulted in a temporary improvement. At 12 months of age, an upper endoscopy and an ileocolonoscopy were performed because of recurrence of symptoms. They showed a mild antritis and duodenitis as well as some colonic aphtheous lesions, one ulcer in the caecum and a normal terminal ileum. Histology showed a mild ileitis and local cryptitis not directly suggestive for an inflammatory bowel disease. Blood analysis showed mild anemia, inflammation and hypoalbuminemia. Coprocultures were negative. VEOIBD was suspected, even though immunologic and genetic work-up remained negative. She was started on azathioprine, mesalazine and prednisolone with temporary improvement. A stool culture at 14 and 15 months of age was positive for a toxin-producing *Clostridium difficile*. She received metronidazole and vancomycine consecutively with temporary improvement. An ileocolonoscopy performed at the age of 16 months showed diffuse aphtheous lesions, deep and superficial ulcers and a normal terminal ileum. Cryptitis, cryptabscesses and cryptdestruction confirmed the VEOIBD diagnosis. *Clostridium difficile* was eradicated. Azathioprine, mesalazine and prednisolone were stopped. Infliximab was started at the age of 16 months (10 mg/kg week 0, 10 mg/kg week 2 and 15 mg/kg week 6) but failed to improve symptoms. Levels remained low and anti-TNF antibodies developed. Methotrexate was tried at 18 months without effect. Transfusion dependent anemia and severe failure to thrive remained with unchanged lesions on an ileocolonoscopy performed at the age of 19 months. Ustekinumab in compassionate use was requested to Janssen and this new treatment could be started. An induction dose of 65 mg ustekinumab IV at the age of 19 months was administered followed by a maintenance dose of 45 mg SC every 8 weeks up to now. Through levels after the third and fourth maintenance doses were respectively < 0.3 and 0.7 µg/ml. Stool consistency and blood loss improved progressively after the third maintenance dose. Growth resumed. Despite persistent mild inflammatory laboratory values, hemoglobin and albumin were corrected and an ileocolonoscopy showed only superficial ulcers in the sigmoid and caecum with mild chronic inflammation on histology after the fourth maintenance dose. After 5 doses of ustekinumab, we can state that this treatment was successful for this infant with a VEOIBD.



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