**Growth failure is rare in a contemporary cohort of paediatric inflammatory bowel disease patients**

Short title- Growth is preserved in paediatric IBD

James J Ashton1,2, Zachary Green1, Aneurin Young3,4, Florina Borca3, Tracy Coelho1, Akshay Batra1, Nadeem A. Afzal1, Sarah Ennis2, Mark J Johnson3,4 and R Mark Beattie1

1. Department of Paediatric Gastroenterology, Southampton Children’s Hospital, Southampton, UK
2. Department of Human Genetics and Genomic Medicine, University of Southampton, Southampton, UK
3. NIHR Southampton Biomedical Research Centre, University Hospital Southampton, Southampton, UK
4. Department of Neonatal Medicine, Southampton Children’s Hospital, University Hospital Southampton NHS Foundation Trust

Correspondence to

Professor R Mark Beattie,

Department of Paediatric Gastroenterology,

Southampton Children’s Hospital

Tremona road,

Southampton,

SO16 6YD,

UK

Mark.beattie@uhs.nhs.uk

**Acknowledgements-** JJA is funded by an Action Medical Research, Research Training fellowship and an ESPEN fellowship. This study is supported by the National Institute for Health Research through the NIHR Southampton Biomedical Research Centre. MJJ and RMB are supported by the National Institute for Health Research through the NIHR Southampton Biomedical Research Centre

**Conflicts of interest-** The authors declare no conflicts of interest

Word count- 3376

Abstract word count- 200

**Abstract**

Aim- We assessed growth in a paediatric inflammatory bowel disease (PIBD) cohort.

Methods- PIBD patients were eligible if they were diagnosed at Southampton Children’s Hospital from 2011-2018. Weight and height standard-deviation-scores (SDS) were retrieved. Mean SDS-values, SDS-change and anti-TNF status were analysed at diagnosis and during follow-up.

Results- 490 patients were included, 313 with Crohn’s disease (CD). CD patients presented with mean height-SDS -0.13, -0.1 at 1-year, -0.11 at 2-years and -0.03 at 5-years, reflecting preserved linear growth. There was no significant height-SDS change from diagnosis to 5-year follow-up, +0.12, 95%-CI 0.48 to -0.24. Mean weight-SDS at diagnosis was -0.39, driven by CD patients (-0.65). Mean weight-SDS approached 0 after 1-year and remained at the 50th-centile throughout follow-up. Growth in ulcerative colitis was maintained.

In multivariable regression males had worse height growth from diagnosis to transition (p=0.036). Anti-TNF treatment (p=0.013) and surgical resection (p=0.005) were also associated with poorer linear growth. Patients treated with anti-TNF therapy had lower height-SDS compared to those never treated with anti-TNF at 1-year (-0.2 vs -0.01, p=0.22), 2-years (-0.27 vs -0.01, p=0.07) and 5-years (-0.21 vs 0.25, p=0.051).

Conclusion- Height was generally maintained in Crohn’s disease and impaired linear growth was rare in this cohort.

Keywords- Paediatric; inflammatory bowel disease; Crohn’s disease; growth; weight; height; anti-TNF

Abbreviations

IBD- inflammatory bowel disease

SDS- standard deviation score

cSDS- change in standard deviation score

Anti-TNF- anti tumour necrosis factor alpha

BMI- body mass index

Key notes

* Historically paediatric Crohn’s disease patients have presented with growth failure, reflected by low weight and height standard deviation scores
* Our cohort does not exhibit linear growth failure at diagnosis, although a deficit in weight remains
* Growth throughout follow-up is largely within normal limits, with weight recovering by 1-year and although anti-TNF therapy was associated with poorer linear growth this is likely to reflect it’s use in more severe disease

**Introduction**

Poor weight gain and impaired growth are characteristic of paediatric inflammatory bowel disease (IBD) in previously reported cohorts, with Crohn’s disease frequently presenting with low weight and height, reflecting growth delay 1. Historically, for many patients, this growth deficit has persisted throughout childhood, associated with impaired nutrition and reduced final adult height 2. Data from the 1980s, 1990s and 2000s reported average standard deviation scores of -0.94 to -1.30 for weight and -0.5 to -1.11 for height at presentation of paediatric Crohn’s disease 3–6. Recently, growth is better maintained with more contemporary treatment, even in disease with onset prior to puberty 7,8. In contrast, ulcerative colitis does not appear to impact on weight or height at diagnosis, or during follow-up, although frequent steroid courses are known to promote adiposity, abnormal body composition and impair growth 8,9.

Control of inflammatory disease activity is key to treating patients with IBD, however it is also important to ensure healthy growth in these children in order to minimise the long-term health implications of undernourishment or obesity 10. Whilst many patients will present underweight, treatments such as repeated courses of steroids, alongside Western diets, may promote adiposity in up to 40% of patients 9,10. Some patients will maintain normal weight gain and linear growth, whilst some, with more severe disease, will continue to be underweight, malnourished and have linear growth failure (stunting) 11.

In Crohn’s disease growth is a particularly important proxy of inflammatory control, adequate nutrition, and delivery of energy and protein requirements 12,13. Whilst growth failure is multifactorial and may be due to systemic inflammation or inadequate nutritional intake, achieving disease control is likely to positively impact on long-term growth2. Anti-TNF therapy is now routine practice in paediatric disease following introduction in the 2000s 14. Therapy appears to have impacted on the number of intestinal resections performed during childhood and has proven efficacy in inducing mucosal healing 15–17. Whether this has translated to an improvement in linear growth is less certain.

This study primarily aimed to assess growth in a contemporary population of IBD patients at diagnosis and through follow-up and assess the impact of treatment on growth outcomes. In addition, we aimed to assess the utility of electronic growth records in assessment of long-term growth for children with chronic disease.

**Methods**

Patients were eligible for inclusion if they were diagnosed at Southampton Children’s Hospital (tertiary centre) at any time from 01/01/2011 to 31/12/2018, and had a confirmed diagnosis of inflammatory bowel disease (Crohn’s disease, ulcerative colitis or IBD-unclassified) in line with the Porto, or modified Porto, criteria 18,19. All patients were aged less than 18 years of age at diagnosis. Height, weight and body mass index (BMI), alongside calculated SDS, were automatically extracted from the electronic patient records (growth charts) at Southampton. Electronic growth charts were introduced in 2011 and data extracted for this project was extracted from 01/01/2011 to 12/08/2019. All SDS are based on world health organisation (WHO) growth charts 20.

Data on anti-TNF therapy and surgical resections, including age at commencement/surgery, were automatically extracted from online medical records16.

Growth measurements

Data were filtered in order to exclude physiologically implausible values, with SDS of > 5 or < -5 for height or weight. Only measures taken when patients were aged less than 18 years were included.

All height and weight measures are performed by trained staff using regularly calibrated equipment. Height and weight measures are manually inputted into the electronic growth record. Growth measures were categorised as follows: to be classified as ‘at diagnosis’, measures must have been taken 3 months prior to diagnosis until 7 days following diagnosis. For ‘at 1-year’ the measurements must have been taken at 12 months +/- 3 months, ‘at 2-years’ measurements must have been taken 24 months +/- 3 months, and ‘at 5-years’ measurements must have been taken at 60 months +/- 6 months. Height and weight-SDS at transition to adult was defined as the last measure of growth at age 16 or 17 years. As the majority of patients transition to regional adult hospitals in Southern England between 17 and 18 years of age, growth data is not routinely available following transition.

Change in SDS (cSDS), between diagnosis and at each time-point, were calculated to demonstrate individual growth outcomes. cSDS was calculated by subtracting the SDS at diagnosis from the SDS at follow-up, with a positive value indicating an increase in growth centile. cSDS data were also used to assess differences in growth before and after introduction of anti-TNF therapy. In order to assess the impact of anti-TNF therapy in patients we utilised growth measures prior to anti-TNF commencement and measures at transition. Where there was no time gap between diagnosis and starting anti-TNF therapy, or no time gap between growth measure at transition to adult care and starting anti-TNF therapy these measures were excluded from further analysis as we were unable to assess cSDS in these patients. Pragmatically, growth measures must have been in the 3 months preceding the commencement of anti-TNF therapy to be included in this analysis.

Data quality control

Due to a graduated change from paper to electronic growth charts in the initial years of this study we retrieved weight and height data at diagnosis from paper medical records to ensure patients without electronic growth parameters were representative of the whole cohort. As this study aimed to standardise data collection using automatic and prospectively entered growth measures these manually curated data were not included in the overall analysis.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess the distribution of the data against a normal distribution. Differences between growth in groups and timepoints were assessed using a T-test.

Linear regression was used to predict growth outcomes (height and weight) at transition to adult care (maximal follow-up) in Crohn’s disease patients. Patients must have been diagnosed for >1 year at transition to adult care to be included. The dependant variables were change in height or weight-SDS from diagnosis to transition to adult services (age 16 or 17 years). Independent variables planned for inclusion in this analysis a priori were age at diagnosis, sex, treatment with anti-TNF therapy (ever) and intestinal surgery (ever) and change in height or weight-SDS (depending on the model). Analyses were conducting using SPSS v25 (IBM).

SDS distribution curves

To assess IBD height and weight in the context of normal growth, histograms and normal distribution curves were produced for Crohn’s disease and ulcerative colitis, at diagnosis and follow-up.

Ethical approval

This study was not considered to be a research study requiring external ethics approval by the United Kingdom Health Research Authority. It was registered locally at University Hospital Southampton as service evaluation (August 2019).

**Results**

Following data quality filtering, 490 patients (313 with Crohn’s disease, 157 with ulcerative colitis and 20 with IBDU) were included in the analysis, with a total of 7246 weight-SDS and 5247 height-SDS measures. Overall, 33.9% of patients with Crohn’s disease, and 48.9% of ulcerative colitis, patients were female. The distribution of the data were normal and therefore mean values were used for comparison of groups (Table S1). The mean age at diagnosis was 12.87 years for Crohn’s disease, 13.02 years for ulcerative colitis and 12.79 years for IBDU.

SDS at diagnosis and follow-up

At diagnosis 373 patients had weight measures and 304 patients had height measures suitable for analysis (Table 1). Mean SDS were calculated for IBD patients, Crohn’s disease patients and ulcerative colitis patients, at diagnosis and each follow-up time-point. Patients diagnosed in 2011 had electronic height or weight measures in only 17/53 (32%) cases. This increased year on year- 48% (2012), 80% (2013), 85% (2014), 85% (2015), 80% (2016), 92% (2017) and 94% (2018). Figure 1a demonstrates the distribution of patients with height and weight measures at diagnosis.

Mean weight at diagnosis was reduced in the IBD cohort (SDS -0.39), driven by a lower mean SDS in Crohn’s disease patients (SDS -0.65). During follow-up mean weight increased, moving closer to an SDS of 0 (50th centile) for Crohn’s disease patients, at 1-, 2- and 5-years following diagnosis. There were significant increases in weight-SDS between diagnosis and 1-year in IBD (SDS -0.39 to 0.1, p=<0.00001), Crohn’s disease (SDS -0.65 to -0.03, p=<0.00001) and ulcerative colitis (SDS 0.16 to 0.42, p=0.045), figure S1a. Following diagnosis, ulcerative colitis patients had a mean weight-SDS consistently > 0.42. At 5-year follow-up mean weight-SDS for ulcerative colitis was 0.91.

Mean height-SDS was not reduced at any time-point for any disease subtype, including at diagnosis, figure S1b. Crohn’s disease patients were consistently shorter, as measured by mean SDS, than ulcerative colitis patients but remained within an SDS range close to zero; -0.12 at diagnosis, -0.1 at 1-year, -0.11 at 2-years and -0.03 at 5-years. There were no significant changes in mean height-SDS in any disease subtype between diagnosis and 1-year, 1-year and 2-years or 2-years and 5-years. At diagnosis 81.5% of patients with weight measures also had height measures.

The percentage of patients with a weight-SDS below -2.0 was calculated (WHO criteria for moderate malnutrition). In a normal healthy population 2.5% of children would fall below the SDS -2.0. At diagnosis 11.8% of all IBD patients were below SDS -2.0 for weight, driven by 16.8% of Crohn’s disease who were below -2.0. Table 1. During follow-up the number of Crohn’s disease patients with moderate malnutrition reduced to 5.1% at 1-year, 3.5% at 2-years and 4.9% at 5-years.

The percentage of patients with a height-SDS below -2.0 was calculated (WHO criteria for moderate stunting). Despite the near-normal mean height-SDS, stunted individuals were over-represented at diagnosis, with 6.4% of Crohn’s disease patients being stunted, which reduced during follow-up to 3.7% at 1-year, 1.4% at 2-years and 1.9% at 5-years. Table 1.

Manually curated growth data

To further ensure patients without electronic growth records did not bias prospectively entered data manually curated weight and height data from diagnosis was compared to the electronic records. Considering Crohn’s disease an additional 44 patients had weight measures and 39 had height measures. Mean weight-SDS was -0.55 and mean height was -0.3. Neither was statistically different from electronic data, p=0.35 and p=0.21 respectively. Considering ulcerative colitis, there were an additional 28 weight measures and 20 height measures. Mean weight-SDS was 0.18 and mean height was 0.09. Neither was statistically different from electronic data, p=0.47 and p=0.18 respectively.

Change in SDS from diagnosis through follow-up

Utilising patients who had consecutive measures from diagnosis through follow-up allowed assessment of average growth in individuals, rather than in the overall cohort. Mean change in weight-SDS from diagnosis to 1-year was +0.51 (264 patients), whereas for height-SDS it was +0.004 (191 patients). The positive change in weight-SDS was consistent throughout follow-up and was driven by positive SDS changes in Crohn’s disease patients, table 2 and figure 1b.

Change in height-SDS was 0 +/-0.12 for both IBD, Crohn’s disease and ulcerative colitis at all time-points (other than ulcerative colitis from diagnosis to 5 years where only 3 patients were included), indicating no overall change in linear growth over time, consistent with a normal distribution at diagnosis.

There was a subgroup of 43 Crohn’s disease patients presenting with weight SDS <2.0 at diagnosis. Of these patients 23 had weight-SDS at transition to adult care, mean weight-SDS was -1.56. Only 6 patients (26.1%) of those with data at transition remained with a weight-SDS <2.0.

Considering height, a subgroup of 14 Crohn’s disease patients presenting with weight SDS <2.0 at diagnosis. Of these patients only 5 had height-SDS at transition to adult care, mean height-SDS was -1.62. Two of the five patients (40%) with data at transition remained with a weight-SDS <2.0.

Impact of treatment on growth in Crohn’s disease

Data were analysed to assess the impact of concurrent anti-TNF therapy on growth. Over the study period 30% of Crohn’s disease patients were treated with anti-TNF therapy (infliximab or adalimumab) at any point. Crohn’s disease patients with growth measures at 1-, 2- and 5-years were categorised into anti-TNF therapy or no anti-TNF therapy at that time-point (based on having received active or past-treatment on the date of growth measurement)16. Mean SDS were calculated for each group, at each time-point. Table 3.

Mean weight-SDS moved towards 0 in both groups, although anti-TNF treated patients returned to the 50th centile by 2 years, compared to 1-year for those not treated with anti-TNF therapy. figure S2a. Mean height-SDS remained normal, or > 0, in patients not treated with anti-TNF therapy. Those patients treated with anti-TNF therapy had mean height-SDS scores of -0.2 at 1 year, -0.27 at 2 years and -0.21 at 5 years. figure S2b.

In order to assess whether this reduction in height and weight was driven by patients who had lower weight and height-SDS at diagnosis, reflecting a more severe phenotype, we assessed the weight and height-SDS at diagnosis of patients who were placed on anti-TNF therapy within 1-year post-diagnosis. The mean weight-SDS for this group (48 patients) was -0.88, whereas for those not treated within the first year the mean weight-SDS was -0.59, p=0.09. The mean height-SDS (38 patients) was -0.22 for those treated at 1-year with anti-TNF, compared to a height-SDS of -0.11 in those not treated with anti-TNF, p=0.29.

We compared change in weight and height-SDS from diagnosis to starting anti-TNF therapy to change from starting anti-TNF therapy to transition in Crohn’s disease. Change in weight-SDS was greater from diagnosis to starting an anti-TNF, mean cSDS +0.4 (44 patients), compared to after starting to transition, mean cSDS +0.08 (25 patients), p=0.003. In contrast change in height-SDS from diagnosis to starting an anti-TNF, mean cSDS -0.03 (26 patients), was not significantly different compared to after starting therapy until transition, mean cSDS +0.05 (15 patients), p=0.47. Figure 1c.

Factors associated with Crohn’s disease growth at maximal follow-up

In order to assess factors associated with Crohn’s disease growth from diagnosis to transition multivariate linear regression analyses were conducted. Change in weight and height-SDS was available for 118 and 74 patients with Crohn’s disease, respectively. A positive relationship between independent and dependant variables equates to a positive impact on growth.

Considering the height model, positive change in height-SDS was predicted by positive change in weight-SDS from diagnosis to transition, beta 0.455 (p=<0.0001). Female sex also had a positive impact on change in height-SDS, beta 0.218 (p=0.036). Conversely, change in height-SDS was negatively associated with anti-TNF therapy, beta -0.269 (p=0.013), having undergone surgical resection during childhood, beta -0.291 (p=0.005) and age at diagnosis, beta -0.237 (p=0.026).

In the weight model, change in weight-SDS was positively predicted by positive change in height-SDS from diagnosis to transition, beta 0.513 (p=<0.0001), with use of anti-TNF also reaching positive significance in this model, beta 0.276 (p=0.017).

SDS distribution curves

Histograms and distribution curves were produced for weight and height in Crohn’s disease and ulcerative colitis at diagnosis, 1-year and 2-years follow-up, figure S3.

**Discussion**

This study presents growth measures at presentation and follow-up in a cohort of 490 paediatric IBD patients treated with contemporary therapy in an established referral network, collated through a standardised electronic recording methodology. These data demonstrate a weight deficit at diagnosis in paediatric Crohn’s disease, which returns towards SDS 0 over the first year of treatment, remaining at or near to the 50th centile (SDS 0) at 2- and 5-years post-diagnosis. In contrast to previous data there was no overall height deficit in the Crohn’s disease cohort at diagnosis or during follow-up. Patients with more severe disease, as assessed by treatment with anti-TNF therapy, did have, on average, a mild height deficit. Linear growth in Crohn’s disease, as measured by change in height-SDS from diagnosis to transition, was negatively associated in a regression model with anti-TNF therapy and surgical resection. Female sex and younger age at diagnosis are positive influences on overall linear growth.

Growth failure has been variably defined in IBD over the last 30 years but includes stunting (height-SDS <-2.0), reduced final adult height, and weight-SDS <-2.0 20,21. Previous data has described growth failure at presentation in paediatric-onset Crohn’s disease, with SDS at diagnosis ranging from -0.94 to -1.30 for weight and -0.5 to -1.11 for height 4,5,21,22. Additionally, this growth failure persisted throughout treatment, observed in 23% of children with IBD the 1990s 23. Puntis *et al* described a cohort of 67 children with Crohn’s disease in the 1980s, reporting 15% with permanent growth and height failure, whilst Sawczenko *et al* reported 19% of their cohort achieving a final adult height of >8cm below their mid-parental target height 21,24. In another, more recent study from Lee *et al*, final adult height was reduced in 11.3% of the cohort 25. Multiple studies report growth failure at presentation being associated with a longer delay between symptom onset and diagnosis, with final height outcomes being closely related to presenting height-SDS 21,26. Our data suggests that weight malnutrition or height stunting, as assessed by WHO criteria (SDS <-2.0), is rare during treatment, with only 4.9% (weight-SDS <-2.0) and 1.9% (height-SDS <-2.0) of Crohn’s disease patients having this at 5-years.

Our data suggests that height at diagnosis, and at 1-, 2- and 5-year follow-up points, is well maintained in Crohn’s disease. In a subset of patients treated with anti-TNF therapy there was a mild deficit (height-SDS -0.2 to -0.27) during follow-up, which did not worsen over time. Previous data has suggested that anti-TNF agents prevent linear growth failure, without restoring patients to their overall growth potential 7. Studies including pubertal staging have reported improved height-SDS with infliximab in children with Tanner stage I-III (+0.5), compared to no change in Tanner stage IV (+0.02), promoting anti-TNF use in pre-pubertal children to restore growth, providing patients are treated in a timely fashion 27,28. Importantly, infliximab has also been associated with increases in lean mass and fat mass in paediatric patients with Crohn’s disease, promoting restoration of normal body composition29. These data may infer that an early, top-down, approach with anti-TNF therapy would result in improved growth, although further data is required to confirm this.

The reasons underlying the lack of a significant deficit in linear growth in this cohort may be numerous. Improved local referral pathways, and standardisation of investigations and treatments have seen overall improvements in the care of paediatric IBD 30. The rise in awareness may be promoting earlier diagnosis, prior to an overall reduction in height-SDS. Patients are increasingly treated with early anti-TNF therapy and have early and continued dietetic input.

This study has several strengths including large numbers of patients and a single centre approach, with access to all contemporary diagnostic and management options. Our data have several limitations, we were unable to include information on pubertal staging to assess possible pubertal delay and stratify by pubertal stage at diagnosis. We were unable to accurately collate Paris classification or steroid courses in the preceding 12 months. We do not have access to specific indications for starting anti-TNF therapy for all patients. As patients transition to adult services the number of patients with 5-year follow-up is low, reflected by loss to follow-up of these patients. Although in excess of 7000 weight and 5000 height measures were available, in order to standardise the data we chose to use a limited number of these measures at specific follow-up points. We manually searched for growth measures in patients not recorded on the electronic growth record at diagnosis, resulting in 68 additional weight measures and 59 height measures. The mean of these measures was not statistically different from electronically curated data, indicating that by excluding patients without electronic growth records we did not bias our data to be reflect more severe or more mild growth failure. At least some of the missing data at diagnosis is due to children being initially seen at outreach clinics in hospitals within our care network. As we do not have access to the electronic systems from all hospitals, growth data collected at these sites would not be included.

Conclusion

There was no overall height deficit in patients presenting with Crohn’s disease in our contemporary cohort. Weight was below average at diagnosis but had recovered to the 50th centile by 1-year. Linear growth failure was rare during follow-up, although some patients did continue to have a mild height deficit. Enabling national data collection on growth in IBD should enable personalised nutrition and assessment of dietary treatment on growth.

**Tables and Figures**

**Table 1**- Height and weight standard deviation scores for inflammatory bowel disease at diagnosis, 1-year, 2-years and 5-years follow-up.

**Table 2**- Change in height and weight standard deviation scores between diagnosis and follow-up

**Table 3**- Height and weight standard deviation scores for Crohn’s disease patients treated with and without anti-TNF at 1-year, 2-years and 5-years follow-up.

**Figure 1A**- Individuals with height (x axis) and weight (y axis) measures at diagnosis. Red represents patients with Crohn’s disease, green is ulcerative colitis and orange is IBDU. Mean values for Crohn’s disease (red) and ulcerative colitis (green) are shown with 95% confidence intervals. Patients lying in the left lower quadrant have height and weight-SDS below 0, similarly patients in the right upper quadrant have weight and height-SDS above 0. Patients with a normal height for weight (representing a proxy of BMI) would lie on a diagonal line running from the left lower quadrant to the right upper quadrant.

**Figure 1B**- Change in weight and height standard deviation scores from diagnosis to follow-up (1-year, 2-years and 5-years). Mean is represented by the dotted line, median represented by the solid line.

**Figure 1C**- Mean change in weight and height standard deviation scores in Crohn’s disease patients treated with anti-TNF therapy from diagnosis to starting anti-TNF therapy, and from starting anti-TNF therapy to transition. Mean is represented by the dotted line, median represented by the solid line.

**Figure S1a** - Mean overall weight standard deviation scores at diagnosis and follow-up. Blue represents all IBD, red is Crohn’s disease and green is ulcerative colitis

**Figure S1b -** Mean overall height standard deviation scores at diagnosis and follow-up. Blue represents all IBD, red is Crohn’s disease and green is ulcerative colitis

**Figure S2a** - Mean weight standard deviation scores at diagnosis and follow-up in Crohn’s disease patients treated with and without anti-TNF therapy. Red represents Crohn’s disease patients who are actively or historically treated with anti-TNF therapy at that follow-up time-point, blue represents patients not treated with anti-TNF at that time-point. The dotted lines represent the trajectory from the mean weight-SDS at diagnosis for patients treated with anti-TNF at 1-year (SDS -0.88, red) and those not treated at 1-year (SDS -0.59, blue), there is no significant difference between the groups, p=0.09.

**Figure S2b**- Mean height standard deviation scores at diagnosis and follow-up in Crohn’s disease patients treated with and without anti-TNF therapy. Red represents Crohn’s disease patients who are actively or historically treated with anti-TNF therapy at that follow-up time-point, blue represents patients not treated with anti-TNF at that time-point. The dotted lines represent the trajectory from the mean height-SDS at diagnosis for patients treated with anti-TNF at 1-year (SDS -0.22, red) and those not treated at 1-year (SDS -0.11, blue), there is no significant difference between the groups, p=0.29.

**Figure S3**- Weight (red and green) and height (blue and pink) standard deviation score histograms for Crohn’s disease (top row) and ulcerative colitis (bottom row). Standard deviation scores were binned automatically, y-axis represents relative frequency (percentage). Distribution curves are superimposed over the histograms. The number of patients in each histogram can be seen in table 1. A standard deviation score of 0.0 is represented by the dotted line, normally distributed growth data would plot a distribution curve with the zenith at this 0.0 line. A shift of the curve to the left indicates an underweight or short population, a shift to the right indicates an overweight or tall population.

**References**

1. Pfefferkorn, M. *et al.* Growth Abnormalities Persist in Newly Diagnosed Children With Crohn Disease Despite Current Treatment Paradigms. *J. Pediatr. Gastroenterol. Nutr.* **48**, 168–174 (2009).

2. Gasparetto, M. & Guariso, G. Crohn’s disease and growth deficiency in children and adolescents. *World J. Gastroenterol.* **20**, 13219–33 (2014).

3. Sawczenko, A., Ballinger, A. B., Savage, M. O. & Sanderson, I. R. Clinical Features Affecting Final Adult Height in Patients With Pediatric-Onset Crohn’s Disease. *Pediatrics* **118**, 124–129 (2006).

4. Sawczenko, a. Presenting features of inflammatory bowel disease in Great Britain and Ireland. *Arch. Dis. Child.* **88**, 995–1000 (2003).

5. Cameron, F. L. *et al.* Clinical progress in the two years following a course of exclusive enteral nutrition in 109 paediatric patients with Crohn’s disease. *Aliment. Pharmacol. Ther.* **37**, (2013).

6. Griffiths, A. M., Nguyen, P., Smith, C., MacMillan, J. H. & Sherman, P. M. Growth and clinical course of children with Crohn’s disease. *Gut* **34**, 939–43 (1993).

7. Bamberger, S. *et al.* Growth and Adult Height in Patients with Crohn’s Disease Treated with Anti-Tumor Necrosis Factor α Antibodies. *PLoS One* **11**, e0163126 (2016).

8. Cameron, F. L. *et al.* Disease Status and Pubertal Stage Predict Improved Growth in Antitumor Necrosis Factor Therapy for Pediatric Inflammatory Bowel Disease. *J. Pediatr. Gastroenterol. Nutr.* **64**, 47–55 (2017).

9. Ashton, J. J. *et al.* Presenting phenotype of paediatric inflammatory bowel disease in Wessex, Southern England 2010-2013. *Acta Paediatr.* **104**, (2015).

10. Singh, S., Dulai, P. S., Zarrinpar, A., Ramamoorthy, S. & Sandborn, W. J. Obesity in IBD: epidemiology, pathogenesis, disease course and treatment outcomes. *Nat. Rev. Gastroenterol. Hepatol.* **14**, 110–121 (2017).

11. Vasseur, F. *et al.* Nutritional Status and Growth in Pediatric Crohn’s Disease: A Population-Based Study. *Am. J. Gastroenterol.* **105**, 1893–1900 (2010).

12. Levine, A. *et al.* Comparison of outcomes parameters for induction of remission in new onset pediatric Crohn’s disease: evaluation of the porto IBD group ‘growth relapse and outcomes with therapy’ (GROWTH CD) study. *Inflamm Bowel Dis* **20**, 278–285 (2014).

13. Wiskin, A. E. *et al.* Nutritional perspectives of children with Crohn’s disease: a single-centre cohort observation of disease activity, energy expenditure and dietary intake. *Eur J Clin Nutr* **70**, 1132–1137 (2016).

14. Ashton, J. J., Batra, A. & Beattie, R. M. Paediatric inflammatory bowel disease- brief update on current practice. *Paediatr. Child Health (Oxford).* **0**, (2018).

15. Civitelli, F. *et al.* Looking Beyond Mucosal Healing: Effect of Biologic Therapy on Transmural Healing in Pediatric Crohn’s Disease. *Inflamm Bowel Dis* **22**, 2418–2424 (2016).

16. Ashton, J. J. *et al.* Increased prevalence of anti-TNF therapy in paediatric inflammatory bowel disease is associated with a decline in surgical resections during childhood. *Aliment. Pharmacol. Ther.* (2019). doi:10.1111/apt.15094

17. Bouguen, G. *et al.* Treat to target: a proposed new paradigm for the management of Crohn’s disease. *Clin. Gastroenterol. Hepatol.* **13**, 1042–50.e2 (2015).

18. Levine, A. *et al.* The ESPGHAN Revised Porto Criteria for the Diagnosis of Inflammatory Bowel Disease in Children and Adolescents. *J Pediatr Gastroenterol Nutr* **58**, 795–806 (2013).

19. IBD Working Group of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition. Inflammatory bowel disease in children and adolescents: recommendations for diagnosis--the Porto criteria. *J. Pediatr. Gastroenterol. Nutr.* **41**, 1–7 (2005).

20. de Onis, M., Garza, C., Onyango, A. W., Rolland-Cachera, M. F. & pédiatrie, le C. de nutrition de la S. française de. [WHO growth standards for infants and young children]. *Arch Pediatr* **16**, 47–53 (2009).

21. Sawczenko, A., Ballinger, A. B., Savage, M. O. & Sanderson, I. R. Clinical Features Affecting Final Adult Height in Patients With Pediatric-Onset Crohn’s Disease. *Pediatrics* **118**, 124–129 (2006).

22. Griffiths, A. M., Nguyen, P., Smith, C., MacMillan, J. H. & Sherman, P. M. Growth and clinical course of children with Crohn’s disease. *Gut* **34**, 939–43 (1993).

23. Motil, K. J., Grand, R. J., Davis-Kraft, L., Ferlic, L. L. & Smith, E. O. Growth failure in children with inflammatory bowel disease: A prospective study. *Gastroenterology* **105**, 681–691 (1993).

24. Puntis, J., McNeish, A. S. & Allan, R. N. Long term prognosis of Crohn’s disease with onset in childhood and adolescence. *Gut* **25**, 329–36 (1984).

25. Lee, J. J. *et al.* Final adult height of children with inflammatory bowel disease is predicted by parental height and patient minimum height Z-score. *Inflamm. Bowel Dis.* **16**, 1669–77 (2010).

26. Ricciuto, A. *et al.* Diagnostic delay in Canadian children with inflammatory bowel disease is more common in Crohn’s disease and associated with decreased height. *Arch. Dis. Child.* archdischild-2017-313060 (2017). doi:10.1136/archdischild-2017-313060

27. Walters, T. D., Gilman, A. R. & Griffiths, A. M. Linear Growth Improves during Infliximab Therapy in Children with Chronically Active Severe Crohnʼs Disease. *Inflamm. Bowel Dis.* **13**, 424–430 (2007).

28. Church, P. C. *et al.* Infliximab Maintains Durable Response and Facilitates Catch-up Growth in Luminal Pediatric Crohnʼs Disease. *Inflamm. Bowel Dis.* **20**, 1177–1186 (2014).

29. Thayu, M. *et al.* Determinants of changes in linear growth and body composition in incident pediatric Crohn’s disease. *Gastroenterology* **139**, 430–8 (2010).

30. Ruemmele, F. M. *et al.* Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn’s disease. *J Crohns Colitis* **8**, 1179–1207 (2014).