Title – A comparison of the effectiveness of a generic oral nutritional supplement with a specialised formula in the treatment of active paediatric Crohn's Disease

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GA, SE, LB, GB, KA, HG, JM, PH, RD, and ML have no conflicts of interest to declare.

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Authors Contributions

RKR and GA conceived the study. RD, DW, ML, SE, LB acquired the data. RKR, GA, DW, RD, ML, JM, SM, LB, DCW, PH, HG, GB, KA, KG analysed and interpreted the data. DW, RD produced the initial draft and all authors critically reviewed and revised the manuscript. All authors approved the final content.

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Data Availability

The data underlying this article is available on reasonable request to the author.

Summary

This article is a retrospective review from three large tertiary paediatric centres examining differences between an IBD specific formula and a generic oral nutritional supplement as EEN in paediatric Crohn's Disease. No significant differences were noted, including rates of remission, but there is a significant cost saving with the generic formula.

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Abstract

Background – Exclusive enteral nutrition (EEN) is the recommended induction treatment of mild to moderate active paediatric Crohn's Disease (CD). This study compared outcomes of two proprietary polymeric formulas. Treatment effectiveness was examined along with practical aspects of formula delivery and differences in estimated treatment costs.

Methods – Data were retrospectively collected from patients with CD who received a generic oral nutritional supplement (*Fortisip)* across two centres (RCH, Melbourne and RHSC, Edinburgh). This was compared to a prospective cohort (RHC, Glasgow) who used a specialised formula (*Modulen IBD).* The data collected included patient demographics, remission rates, biochemical markers, administration method and anthropometrics. The estimated treatment cost was performed by comparing price per kcal between each formula.

Results – 171 patients were included (106 *Fortisip,* 65 *Modulen IBD,* 70/171 female; median age 13.3 yrs). No difference was demonstrated in remission rate (*Fortisip* n=67/106 [63%] vs *Modulen IBD* n=41/64 [64%], p=0.89), non-adherence rate (*Fortisip* n=7/106 [7%] vs *Modulen IBD* 3/64 [5%], p=0.57) or method of administration (NGT *Fortisip* use n=16/106 [12%] vs *Modulen IBD* 14/65 [22%], p=0.31). There was no difference in reduction of biochemical disease markers between the groups (CRP p=0.13, ESR p=0.49, FC p=0.94). However, there was a cost-saving of around £500/patient/course if the generic oral nutritional supplement was used.

Conclusions – The generic oral nutritional supplement and specialised formulas both had similar clinical effectiveness in induction of remission in paediatric CD. However, there is considerable cost saving when using a generic oral nutritional supplement.

Key Words

Paediatrics

Introduction

Crohn's disease (CD) is the commonest form of inflammatory bowel disease (IBD) in children and adolescents.[1] Weight loss, impaired linear growth and specific nutritional deficiencies are common with many children at first presentation.[2] Current treatments focus on inducing remission of clinical disease, with a growing emphasis placed upon achieving and then maintaining mucosal healing, promoting optimal growth, and minimising the treatment burden and maximising quality of life.[3] Exclusive enteral nutrition (EEN) is the recommended first line treatment for active mild to moderate paediatric CD.[4]

Protocols for the delivery of EEN vary between centres. However, the most recent joint ECCO-ESPGHAN guidelines for the medical management of paediatric CD recommend a 6-8 week course of a polymeric formula.[4] In children, this has been shown to have equal efficacy at inducing clinical remission compared to corticosteroids (CS).[5] Exclusive enteral nutrition has the additional benefit of nutritional rehabilitation, improved mucosal healing and a favourable side effect profile compared to CS.[5] However, remission rates between centres are variable, with reports commonly between 60-80%.[6]

There is wide variation in practice with regards the type of formulation and to a lesser extent the method of administration.[5] A recent extensive analysis compared 61 different proprietary formulas all used successfully for induction of remission in CD. [7] The authors demonstrated considerable variability in macronutrient, non-nutrient ingredients and food additive content between formulas.[7] However, no clear difference in clinical remission rates has been demonstrated between elemental, polymeric and semi-elemental formulas or with the use of different composition and amount of fat.[5] Therefore, important factors that centres

must consider when choosing what formula to use, include availability and supply within their area, cost, ease of use and palatability.

Fortisip (Nutricia, Danone) and *Modulen® IBD* (Nestlé Health Science, Vevey, Switzerland) are both nutritionally complete, polymeric formulas. *Fortisip* is supplied in ready-prepared bottles and is classed as a generic oral nutritional supplement. In contrast *Modulen IBD,* which is described as a specialised IBD formula*,* is supplied in powder form, requiring patients to prepare the formula prior to use. Both enteral nutrition formulas are commonly used worldwide.[7] However, there is a paucity of published data of clinical outcomes following treatment with *Fortisip*, and the clinical effectiveness of both formulas has not been directly compared, particularly when looking at responses to biomarkers of colonic inflammation.[5] The current study compared differences between formulas in clinical remission rates, changes in anthropometry and common disease activity biomarkers (e.g. C reactive protein [CRP], faecal calprotectin [FC]) during treatment. This was done by combining data from three large tertiary paediatric IBD centres including retrospective data from two previously unpublished cohorts and prospective data from a previously published cohort.[8]

Materials and Methods

Generic oral nutritional supplement dataset

The medical records of patients with CD were retrospectively reviewed across two tertiary referral centres. Data were collated from The Royal Hospital for Sick Children, Edinburgh (RHSC) (April 2018 to October 2020) and The Royal Children's Hospital, Melbourne (RCH) (February 2015 to December 2017). Patients who were commenced on *Fortisip* for EEN were included in the study group. Clinical disease activity was assessed using a physician global assessment (PGA). The study assessed rates of clinical remission. Rates of non-compliance and requirement for nasogastric tube (NGT) use were also assessed. Changes in FC, erythrocyte sedimentation rate (ESR) and CRP during treatment with *Fortisip* were also recorded.

Both data sets from the Royal Hospital for Sick Children, Edinburgh and Royal Children's Hospital, Melbourne recorded CRP and ESR prior to commencing EEN (+/- 2 weeks) and on completion of EEN (+/- 2 weeks). Faecal samples for FC measurement were obtained prior to commencing EEN (+/- 4 weeks) and following completion of EEN (+/- 4 weeks).

Within the RHSC cohort the CRP was analysed on an Abbott Architect c16000 using an immunoturbometric assay (Abbott, Abbott Park, Illinois, USA) and FC on the CALP0170Calprotectin (ALP) ELISA (Lysaker, Norway). The RCH FC analysis was performed on the Phadia 250 instrument using the EliA Calprotectin 2 assay (Phadia GmbH, Freiburg, Germany) and CRP on the Vitros systems 250/350/950/5/5600/4600 (Ortho-clinical diagnostics, High Wycombe, UK) .

Specialised formula dataset

Patients undergoing treatment with EEN using *Modulen IBD* were prospectively recruited from October 2014 to May 2017 from the Royal Hospital for Children, Glasgow (RHC). Clinical characteristics of these patients have previously been reported[9]. Patient's clinical disease activity was assessed using the weighted paediatric Crohn's disease activity index (wPCDAI)[10] prior to patients commencing treatment with EEN, and at the end of EEN. Rates of NGT use, anthropometry, clinical biochemistry (CRP and ESR) and changes in FC were recorded. As wPCDAI data was not available in the two retrospective cohorts this was not included in the analysis.

Disease location

The RHSC and RHC assessed disease location using the Paris classification[11], and the RCH disease location using the a modified Paris classification that did not subdivide upper disease according to its relation to the ligament of treitz, including all upper disease as L4. Therefore, to ensure comparability, the current study has reported disease location using this modified Paris classification.

Estimated treatment cost analysis

The estimated treatment cost comparison was completed by assessing the price difference of the formulas (between 2014 – 2020), calculating the daily cost/calories/day and then working out the yearly saving based on median calorie intake, median course length and the number of courses/year in each of the 3 centres. The cost of *Fortisip* (per 200mls bottle) over the years of data collection was £1.40 until 2017, when the price dropped to £1.12 within the UK (these prices were gathered through discussion with the Paediatric Community Account Manager, Specialised Nutrition). The cost of *Modulen IBD* (per 400g tin) was £15.06 until 2017, when the price increased to £15.59. Since 2018 the price has been static at £16.19

(these figures were gathered by correspondence with the Medical Science Liaison, Nestle HealthCare Nutrition). The cost analysis was completed using 2017 prices, as this time cuts across the study period. Each tin of *Modulen IBD* contains 400 g of powdered formula, consisting of 2000 kcals. Each *Fortisip* 200 ml bottle provides 300 kcals. The equivalent cost of *Fortisip* to provide 2000 kcals is £7.47.

Statistics

Descriptive statistics are expressed as median (IQR). Anthropometric data are expressed in z-scores. For comparisons between type of EEN formula used, patients from RHSC and RCH were grouped together and compared against patients treated from RHC. Differences in rates of remission between *formulas* were compared using chi-squared test. Paired data was analysed using a paired t-test. Significance levels were set at a p-value of <0.05. The analysis was carried out on Minitab version 18 statistical software (Minitab Ltd, Pennsylvania, USA).

Ethical Considerations

The Glasgow *Modulen IBD* study[9] was approved by the NHS West of Scotland Research Ethics Committee and registered in clinicaltrials.gov (NCT02341248). The retrospective *Fortisip* study from the Melbourne group was approved by the Human Research Ethics Committee (HREC) based at the Murdoch Research Institute, Melbourne, Australia. In line with local protocol Ethics approval was not sought for the Royal Hospital for Sick Children, Edinburgh, *Fortisip* cohort as this was classed as critical appraisal of practice.[12]

Results

Patient characteristics and clinical remission rates during treatment with exclusive enteral nutrition

The RHSC, *Fortisip* cohort consisted of 60 patients receiving EEN, of whom 42 received *Fortisip*. The RCH, *Fortisip* cohort included 74 patients, of whom 64 underwent an EEN course with *Fortisip*. Sixty-six children were included from the Royal Hospital for Children, Glasgow; one patient was started directly on anti-TNF therapy and was excluded from further analysis. The remaining 65 were treated with *Modulen IBD* and were included in subsequent analysis.

There was no difference in the distribution of patient sex (p=0.32) or age (p=0.767) between the treatment centres (Table 1). There was a significant difference between the proportion of patients undergoing their first course of EEN (RHC: 60/65 [92%] vs RHSC: 24/42 [57%], p<0.001). These data were not recorded within the RCH cohort (see Table 1).

There was no difference in length of EEN treatment between the two EEN formula groups (median [Q1, Q3] EEN days *Fortisip*: 56 d [42, 56] vs *Modulen IBD*: 55 d [45, 56], p=0.78). Patients treated with *Modulen IBD* were prescribed more calories per day than patients treated with *Fortisip* (median [Q1, Q3] prescribed calories/d *Fortisip*: 2100 kcal/d vs *Modulen IBD*: 2400 kcal/d [2000, 2550], p=0.03).

The was no difference in remission rates (p=0.89), failure to achieve remission (p=0.67), non-adherence (p=0.57), or need to insert NGT (p=0.31) between the *Fortisip* and *Modulen IBD* (Table 2). When comparing patients who were receiving a first course of EEN to those receiving a repeat course there was no difference in remission rates when taking all

patients together (p=0.199), and neither were there differences when looking at both formula types (*Fortisip* p=0.194; *Modulen IBD* p=0.424).

Changes in anthropometry during treatment with exclusive enteral nutrition

Prior to treatment initiation there was no difference in weight z-score, height z-score, or BMI z-score between the two EEN formula groups (mean [SD] weight z-score *Fortisip*: -0.78 [1.1] vs *Modulen IBD*: -0.58 [1.2], p=0.264; height z-score *Fortisip*: -0.52 [1.0] vs *Modulen IBD*: -0.19 [1.15], p=0.074; BMI z-score *Fortisip*: -0.73 [1.3] vs *Modulen IBD*: -0.83 [1.36], p=0.65).

By the end of EEN there was no difference in weight z-score and height z-score between the two formula groups (mean [SD] weight z-score *Fortisip*: -0.47 [0.97] vs *Modulen IBD*: -0.25 [0.94], p=0.191; mean [SD] height z-score *Fortisip*: -0.49 [0.98] vs *Modulen IBD*: -0.17 [1.0], p=0.133). At the end of EEN patients treated with Fortisip had lower BMI z-score compared with patients treated with *Modulen IBD* (mean [SD] BMI z-score *Fortisip*: -0.5 [1.1] vs *Modulen IBD*: -0.1 [0.9], p=0.03).

Changes in inflammatory biomarkers during treatment with exclusive enteral nutrition

Prior to treatment initiation, patients treated with *Fortisip* had higher median CRP and ESR levels than patients treated with *Modulen IBD* (median [Q1, Q3] CRP *Fortisip*: 22 mg/L [7, 43] vs *Modulen IBD*: 9 mg/L [3, 24] , p=0.003; ESR *Fortisip*: 29 mm/hr [15, 59] vs *Modulen IBD*: 21 mm/hr [9, 34], p=0.01). However, there was no difference in FC levels between the two groups (median [Q1, Q3] FC *Fortisip*: 1738 mg/kg [969, 3000] vs *Modulen IBD*: 1438 mg/kg [1022, 1824], p=0.06).

By the end of EEN, patients treated with *Fortisip* had higher median CRP values compared with patients treated with *Modulen IBD* (median [Q1, Q3] CRP *Fortisip*: 5 mg/L [5, 14] vs *Modulen IBD*: 3 mg/L [1, 3], p<0.001). There was no difference in the percentage of patients who achieved CRP within normal range (CRP < 7 mg/L) (normal CRP *Fortisip*: n=37/54 [69%] vs *Modulen IBD*: n=29/35 [83%], p=0.13). There was no difference in the median concentration of ESR or FC between the two EEN formula groups (median [Q1, Q3] ESR *Fortisip*: 14 mm/hr [6, 23] vs *Modulen IBD*: 10 mm/hr [5, 21], p=0.491; median FC *Fortisip*: 526 mg/kg [150, 1037] vs *Modulen IBD*: 455 mg/kg [182, 1159], p=0.937).

Estimated cost analysis

The median prescribed calories, across all three centres was 2200 (Q1: 2000, Q3: 2400) kcal/day. To provide this number of calories, the cost of *Fortisip* was estimated at £8.22, while the cost of *Modulen IBD* was £17.15 per day. The median duration of treatment was 56 (Q1: 42, Q3: 56) days, which equates to a price of £460 if using *Fortisip* and £960 if using *Modulen IBD*, giving a median price difference of around £500/patient. Across the three centres studied, the number of courses of EEN varied between 24 courses/year (RHSC) to 26 courses/year (RCH and RHC). This translates into a yearly saving of £12,001– £13,002 if *Fortisip* is used over *Modulen IBD*.

Discussion

The efficacy of EEN is well documented, and should be considered first line treatment for induction of remission in patients with active low-to-moderate risk inflammatory CD (B1),[11] independent of disease location.[4] While many formulas are efficacious, establishing the optimum treatment regimen for each patient while considering factors including palatability and cost is important to maximise compliance and optimise service delivery. There is a relative richness of published literature and clinical experience using *Modulen IBD* as the primary formula in EEN in comparison with *Fortisip* (26 studies vs 1 study)(Supplementary table 1). These studies demonstrate the overall efficacy of EEN and its impact on nutritional parameters, bone density and alteration of the gut microbiome. However, the current multicentre study is one of the first to directly compare 'real life' outcomes between two different polymeric formulations.

While there were differences in resource allocation and service delivery between centres, the median remission rates between centres in our cohorts (57 – 67%) are similar to those in the latest Cochrane meta-analysis by Narula et al. (62 – 83%).[5] This review also compared differences in clinical outcomes between elemental, semi-elemental and polymeric formulas, with no significant difference demonstrated.[5] This is in line with our findings of no significant difference between the preparations in their ability to induce clinical remission. Of note, there was a higher caloric intake in the *Modulen IBD* group, which is reflected in a higher post-EEN median BMI when compared with the *Fortisip* group.

Consistent with existing data, improvements were also demonstrated in biochemical markers of inflammation. CRP significantly reduced during the treatment period with normalisation in the majority of patients. Equal reduction was seen in ESR between the

groups. EEN has been shown to be equally effective as CS at inducing clinical remission in newly diagnosed patients and those who have relapsed, with the additional benefit of greater mucosal healing rates.[13] Faecal calprotectin can be used as a proxy marker for mucosal healing[14] and while our data FC levels significantly improved by the end of the treatment period, they did not normalise in the majority of patients. Incomplete normalisation of FC has been previously demonstrated with EEN.[9] However, this may in part be explained by some samples being taken after EEN completion risking samples being taken from those with rising FC levels during food re-introduction.[8]

The three cohorts had comparable study populations with no significant difference demonstrated in demographics between the groups. The nature of the study in comparing retrospective and prospective cohorts likely introduces bias and the results should be interpreted in this context. However, there was no significant difference between each group and results are consistent with existing data[5], which may be seen as evidence that any affect is low. A potential confounding variable and limitation of the study is the difference in numbers of initial courses versus repeat EEN courses. There was a greater percentage of repeat courses in the RHSC, *Fortisip* cohort, compared to the RHC, *Modulen IBD* group. This data was not recorded in the RCH, *Fortisip* cohort. This may favour a higher response rates in the *Fortisip* group by selecting those who had previously responded and were therefore likely to again. Conversely, decreased efficacy to a second course has previously been demonstrated and may underestimate biochemical marker reduction had the cohort been exclusively newly diagnosed patients.[15] On the subgroup analysis no significant difference was noted in remissions rates which may indicate this variable had a modest, if any, effect on the results.

With little difference in effectiveness between formulas practical aspects need to be carefully considered when deciding on the formula used within a centre including patient adherence factors, funding, cost and availability. Navas-Lopez et al. explored barriers to successful delivery of EEN. These included lack of acceptance from the family, inadequate health resources to provide follow-up and budget limitations.[16] *Fortisip* comes as a pre-made bottle in eight flavours compared to *Modulen IBD* which is a single, vanilla flavoured, powder and requires to be made up prior to use, although flavouring can be added to it and formulas can be concentrated to overcome tolerance issues . While there is limited qualitative studies assessing patient preference, reduced time for preparation of *Fortisip* and ease of transport may be seen as an advantage in promoting patient acceptability and adherence. Future studies should seek this information from patients to see if this theoretical difference is true in clinical practice; however, our results also confirm that some patients are intolerant of oral EEN of any type and can only complete the treatment course with use of an NGT tube. Additionally, as *Fortisip* has a higher standard calorific density concentration than *Modulen IBD* (1.5 kcal/ml vs 1.0 kcal/ml) a smaller volume is required when establishing patients on EEN. If a patient were to require 1800 mls *Fortisip* per day (1800 kcal), the equivalent volume of *Modulen IBD* (at the standard 20% concentation, 1kcal/ml) to give the same number of calories would be 2700 mls per day. This volume is often too great for the majority of patients to manage, therefore the dietetic teams in our centres concentrate the *Modulen IBD* to ensure the volume is manageable e.g. to 25% (1.25 kcal/ml) or 30% conc (1.5 kcal/ml) as tolerated.

Rates of non-adherence and NGT use were comparable between formulations indicating similar degrees of tolerance. The increased post-EEN BMI seen in the *Modulen IBD* group may in part be explained by the greater average prescribed calories. As no significant

difference was demonstrated in rates of NGT tube usage, clinical remission rates or rates of non-adherence we cannot conclude that differences in formula concentration, volume or taste translate to important differences in clinical practice. It is likely that there is a wide range of patient preferences and is may be prudent to offer a number of options in any centre to maximise adherence, this study reinforces this point.

The major significant difference we found between these formulations is in estimated cost. The cost analysis has demonstrated a saving of around £500 per patient per course if *Fortisip* is used over *Modulen IBD*. The yearly saving within an individual centre would clearly depend on the number of EEN courses prescribed each year. This study has highlighted that a theoretical saving can be made with no significant reduction in effectiveness. An established service with experienced dieticians and specialist nurses are fundamental to the successful delivery of EEN and achieving the best outcomes.[4,17] This cost saving could (theoretically at least) increase the resource allocation of the multi-disciplinary team to better support families.

Solid food-based diets including the Crohn's disease treatment with eating (CD-Treat)[18] and the Crohn's disease exclusion diet (CDED)[19] coupled with 50% partial enteral nutrition aim to improve treatment tolerability. However, there is need for more evidence before these are accepted into everyday clinical practice and adopted widely. Additionally, there are high energy/protein dessert style supplements, such as *Forticreme Complete* (Nutricia, Danone), which comes in four difference flavours, and may also improve acceptability if used during an EEN course although these products may require further study before entering routine use.

Conclusion

Exclusive enteral nutrition remains the first line treatment for induction of remission in paediatric CD and optimising treatment regimens is paramount to effective service delivery. Our data has increased departmental confidence in the use of a variety of formulas contributing towards cost savings. However, larger prospective RCT trials would likely provide additional information to optimise EEN regimens. This study provides wider evidence that there is no significant difference in clinical effectiveness between generic nutritional supplements versus IBD specific nutritional supplements and that other factors including convenience, patient measures and cost savings should all be considered by each unit when deciding on the choice of formula(s).

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Table 1 Baseline demographics and phenotypic characteristics of patients with Crohn's disease across three centres

	RHSC (N=42)	RCH (N=64)	RHSC/RCH combined (N=106)	Logan et al (N=65)
Age (yrs)	13.0 (11.3, 15.1)	13.3 (12.0, 15.2)	13.2 (11.6, 15.2)	13.4 (11.0,15.0)
Females	15 (36%)	31 (48%)	46 (43%)	24 (37%)
Initial course	24 (57%)	Not recorded		60 (92%)
Disease Location				
Ileal	5 (12%)	11 (17%)	16 (15%)	6 (9%)
Colonic	12 (29%)	17 (27%)	29 (27%)	24 (36%)
Ileal-colonic	23 (55%)	34 (53%)	57 (54%)	35 (53%)
Isolated upper	2 (5%)	0	2 (2%)	1 (2%)
Isolated perianal	0	2 (3%)	2 (2%)	0
Perianal disease present	8 (19%)	2 (3%)	10 (10%)	6 (9%)

Table 2 Comparison of remission rates and nasogastric tube use between Fortisip and Modulen IBD

	Fortisip (RHSC) N=42	Fortisip (RCH) N=64	Combined Fortisip (RHSC and RCH) N= 106	Modulen IBD (Logan et al) N=65
Remission	24 (57%)	43 (67%)	67 (63%)	41 (63%)
Treatment did not induce remission	14 (33%)	18 (28%)	32 (30%)	22 (33%)
Non-adherence	4 (10%)	3 (5%)	7 (7%)	3 (4%)
Nasogastric Tube inserted	4 (10%)	12 (19%)	16 (12%)	14 (22%)

450 *Table 3 Descriptive statistics of anthropometry and inflammatory biomarkers during exclusive enteral nutrition between centres*

451	Fortisip (RHSC)	Fortisip (RCH)	Combined Fortisip (RHSC and RCH)	Modulen IBD (RHC)	Fortisip (RHSC)	Fortisip (RCH)	Combined Fortisip (RHSC and RCH)	Modulen IBD
	EEN start				EEN End			
Weight z-score	-0.5 [0.91] n=38	-0.98 [1.25] n=55	-0.78 [1.15] n=93	-0.58 [1.11] n=64	-0.19 [0.71] n=24	-0.61 [1.05] n=49	-0.47 [0.97] n=73	-0.25 [0.94] n=53
Height z-score	-0.39 [0.94] n=37	-0.63 [1.1] n=44	-0.52 [1.03] n=81	-0.19 [1.15] n=64	ND	-0.49 [0.98] n=43]	-0.49 [0.98] n=43	-0.17 [1.03] n=52
BMI z-score	-0.53 [1.09] n=37	-0.9 [1.44] n=44	-0.73 [1.3] n=81	-0.83 [1.36] n=64	-0.35 [0.89] n=22	-0.57 [1.22] n=43	-0.5 [1.12] n=65	-0.09 [0.92] n=52
ESR (mm/hr)	23 [9, 25] n=16	35 [16, 65] n=53	29 [15, 58] n=69	21 [9, 34] n=55	14 [6, 20] n=10	14 [6, 25] n=41	14 [6, 23] n=51	10 [5, 21] n=40
CRP (mg/L)	7 [1, 29] n=24	26 [12, 51] n=54	22 [7, 43] n=78	9 [3, 24] n=59	3 [1, 5] n=12	6 [5, 20] n=42	5 [5, 14] n=54	3 [1, 3] n=36
Faecal calprotectin (mg/kg)	1115 [875, 2250] n=20	2238 [1107, 3000] n=30	1738 [969, 3000] n=50	1438 [1022, 1824] n=64	716 [394, 1037]	341 [133, 1191] n=16	516 [150, 1037] n=28	455 [182, 1159] n=37
% underweight	8% (n=3/37)	27% (n=12/44)	17% (n=14/81)	18% (n=12/66)	10% (n=2/22)	16% (n=7/43)	12% (n=8/65)	2% (n=1/52)
% thin (weight > -2SD)	5% (n=2/38)	16% (n=9/55)	12% (n=11/93)	11% (n=7/66)	0% (0.24)	10% (n=5/49)	7% (n=5/73)	6% (n=3/53)

Abbreviations: ND: No data; BMI: Body mass index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; RHSC: The Royal Hospital for Sick Children; RCH: The Royal Children's Hospital; RHC: Royal Hospital for Children. % underweight: BMI > -2SD); % thin: weight > -2SD.

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