RESEARCH PLAN

Modified vs Standard CDED: Evaluation of a Nordic Adaptation of Nutritional Therapy in Paediatric Crohn's Disease

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1. Scientific Question

The aim of this study is to investigate whether a Nordic version of the Crohn's Disease Exclusion Diet (Nordic CDED) is as effective in achieving clinical remission as the original version of the diet, which was developed by Levin A et.al. in 2019 [1].

The primary objective is to compare the clinical effect — in terms of remission rates — between Nordic CDED and results from studies where the original CDED has been used in similar patient groups with comparable methodology.

The secondary objective is to evaluate if a Nordic adaptation of the CDED may facilitate individualization and improve adherence and quality of life in paediatric patients with Crohn's Disease.

2. Overview of the field

Crohn's Disease (CD) has increased in prevalence worldwide over the past decades, particularly among children and young people. In Northern Europe, the prevalence is among the highest in the world, with approximately 0.13% of the population living with Crohn's disease [2]. This disease not only causes significant personal suffering and reduced quality of life for affected individuals, but also leads to increased healthcare costs. Additionally, it has a major impact on patients' dietary habits, social lives, and self-image [3]. Research has not yet fully clarified why CD develops, but it appears to involve a complex interaction between genetic factors, the immune system, gut microbiota, and environmental influences — with diet playing an increasingly important role.

In the 1990s, exclusive enteral nutrition (EEN), consisting of 6–8 weeks on a liquid diet, was shown to induce remission in patients with mild to moderate active Crohn's disease (CD) [4, 5]. While the underlying mechanisms of EEN remains unknown, [5-7] it has been proposed to favourably modulate the gut microbiome,[8] the intestinal barrier function and immunity.[9] In children with mild to moderate CD, EEN remains the first-line treatment recommended by the European Crohn's and Colitis Organization (ECCO), the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) [7], and the Swedish national guidelines [10]. Therefore, this remains a common first-line treatment in the Swedish health-care setting.

However, EEN can be difficult to maintain due to issues such as taste fatigue, poor palatability, nausea, bloating, and the social and psychological burden it places on the patient [4, 11]. As a result, EEN is not considered suitable for long-term management, and many families seek dietary therapies that allow children to eat solid foods.

In recent years, advances in basic and clinical research have greatly expanded our understanding of how dietary factors influence the development and progression of CD. Growing evidence indicates that certain dietary components — particularly ultra-processed foods — may contribute to triggering and maintaining intestinal inflammation in CD [12-15].

In line with this new knowledge, Crohn's Disease Exclusion Diet (CDED) was developed — a dietary treatment that has demonstrated comparable efficacy to EEN in achieving corticosteroid-free remission. CDED combines partial enteral nutrition (PEN) with carefully selected foods. Unlike EEN, it includes real food, making it easier for patients to adhere to the treatment while maintaining a more normal lifestyle. Research since 2014 has shown that CDED can help reduce inflammation and maintain remission over time, both in children and adults [1, 16-20].

CDED was developed to be adaptable across countries and cultures, using simple and internationally accessible foods, but has so far primarily been applied in Western populations. Implementing a diet-based treatment presents significant challenges in different cultural contexts. Factors such as food availability, patient preferences, religious dietary restrictions, the organization of healthcare services, and societal structures — for example, the fact that schools are often responsible for providing children's meals — mean that dietary adjustments are frequently necessary for the treatment to be feasible, acceptable, and safe in practice. To date, published research on experiences with CDED has primarily been conducted in countries such as Israel, Canada, the USA, and Argentina, as well as several European countries including Spain, Ireland, Sweden, Croatia, and Poland, with ongoing studies in, among others, France and the Netherlands. All these studies confirm the effectiveness of the diet, and among the approximately 20 published studies, several report the need for adaptations — primarily related to the availability of enteral nutrition products and unprocessed foods [19, 21-23].

Our experience

Since 2020, we have treated 10 patients with the original CDED at our paediatric unit. While patients appreciated the ability to eat solid foods and experienced improvements in quality of life, many still found the diet difficult to follow due to the limited variety of unprocessed food options, enteral product and the monotony of the protocol. This placed a significant burden not only on the child but also on their family. Based on our experience, the need for a culturally and practically adapted version has become increasingly evident. Expanding the range of permitted whole foods and compatible enteral nutrition products could make the diet feel less restrictive and more viable.

A secondary goal is for families to gain sufficient knowledge by the end of the treatment to adopt a long-term healthy dietary pattern that aligns with their cultural background, habits, and preferences. In doing so, CDED not only supports remission during active disease but also contributes to long-term improvements in dietary quality and overall prognosis.

We have therefore developed a theoretical framework for a Nordic version of CDED (Nordic CDED), aimed at offering a more sustainable, culturally relevant, and patient-centred dietary option for children with Crohn's disease. This work was recently published in the journal *Frontiers in Nutrition* [24].

Study Purpose

The purpose of this study is to evaluate whether a clinical, cultural, and social adaptation of the Crohn's Disease Exclusion Diet (CDED) to Nordic conditions may improve adherence to dietary treatment among children with CD. It is of utmost importance that this adaptation is carried out without compromising the anti-inflammatory principles of the diet. Such an adaptation is expected not only to enhance adherence but also to reduce the negative impact on quality of life and social well-being for the children and families undergoing dietary treatment. With this knowledge, children would have the opportunity to actively influence their health not only during disease flare-ups but also during symptom-free periods. The overarching goal of this nutritional treatment is to improve gut health by excluding pro-inflammatory foods, without restricting the diet more than necessary.

The aim is for a feasible, culturally adapted version of CDED to be incorporated into Swedish IBD treatment guidelines, offering patients additional options for diet-based management. This approach also has the potential to reduce reliance on medications, thereby lowering the risk of side effects and decreasing overall healthcare costs.

If the Nordic version of CDED (Nordic CDED) proves to be clinically equivalent to the original version, it could serve as a model for how dietary treatments can be adapted to different cultural and social contexts. This, in turn, could contribute to improved adherence and thereby greater treatment efficacy for children with CD in other parts of the world as well. The results from this study will contribute to the growing evidence base for dietary treatment in inflammatory bowel disease and support the development of individualized and more sustainable nutritional strategies for this patient group.

3. Project description

Study design

Multicentre, prospective clinical study with historical controls and non-diet treated controls, utilizing a quantitative approach.

Sample Size:
This study is designed as a non-inferiority study with historical controls and non-diet treatment controls. Assuming no true difference between the standard and new intervention (i.e., 70% remission/improvement in both groups), a total of 60 patients (30 per group) is required to ensure with 90% power that the 95% confidence interval for the difference between groups excludes a clinically significant difference of 35% or more.

Study Sites:
Skaraborg Hospital Skövde, Department of Paediatric Medicine. From June 2026 additional patients will be included from Queen Silvia Children's Hospital, Paediatric Gastroenterology Unit (Eastern Hospital, Sahlgrenska University Hospital), North Älvsborg County Hospital, Southern Älvsborg Hospital and Skånes University Hospital.

Participants:
Children aged 6–18 years with newly diagnosed mild to severe Crohn's disease from January 2026, will be recruited from the paediatric gastroenterology clinic at Skövde Hospital. From June 2026, the other remaining hospitals will be included in the study to support recruitment and achieve the required sample size.

Intervention Group:
The selection consists of all children (6–18 years) with newly diagnosed mild to severe Crohn's disease who are candidates for dietary treatment based on the decision by the patient's treating physician.

Historical Control Group (1): Consists of data from previously published studies in which the original CDED has been used in comparable patient groups. These studies should have been conducted with a similar study design, e.g., prospective clinical studies including children with CD treated with CDED in combination with PEN in similar proportions, and where clinical remission was used as the primary outcome measure.

Control Group (2): Patients with Crohn's disease registered in SWIBREG who were not treated with dietary therapy and who are diagnosed during the project's recruitment period.

Inclusion Criteria:

- Children aged 6–18 years
- Recent (<36 months) mild-to-severe CD diagnosis (defined as Paediatric Crohn's Disease Activity Index [PCDAI] 15–47.5)
- Evidence of active inflammation (C-reactive protein [CRP] ≥ 0.5 mg/dL, erythrocyte sedimentation rate [ESR] ≥ 20 mm/h, and/or faecal calprotectin [FCP] ≥ 200 mg/g during screening)
- Stable use of medication other than steroids

Exclusion Criteria:

- Eating disorder (screening method: SCOFF questionnaire)[25]
- Active extraintestinal manifestations
- Use of systemic corticosteroids
- Active perianal disease

- Positive stool cultures for pathogens, parasites, or *Clostridioides difficile*
- Fever >38.3°C
- Documented cow's milk protein allergy
- Diabetes, celiac disease
- Psychosocial difficulties

Outcome Measures

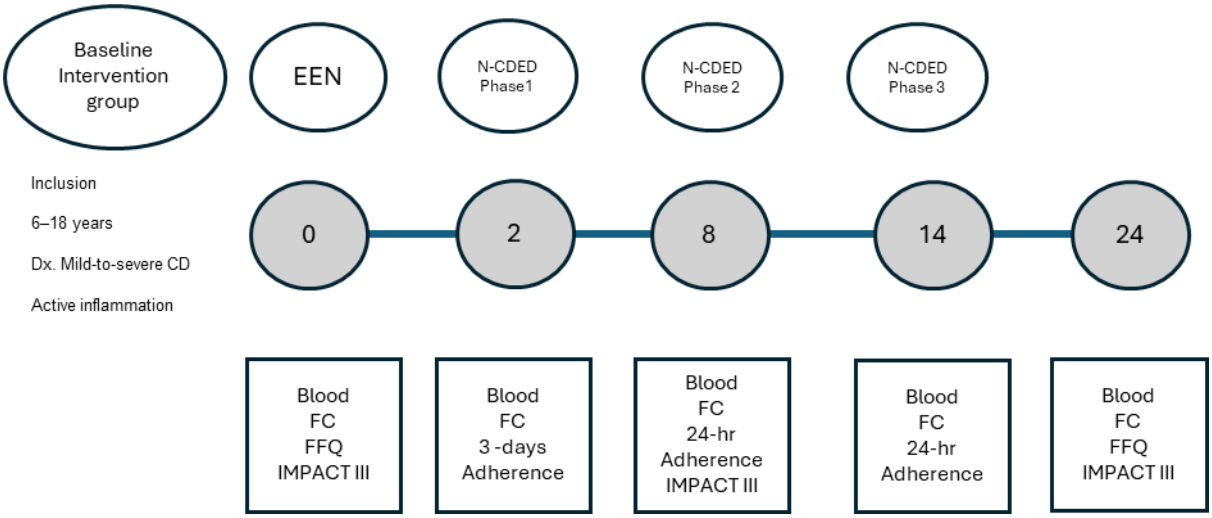
Primary Endpoint:

- Corticosteroid-free clinical remission at week 14 (PCDAI ≤10 without systemic steroid use)

Secondary Endpoints:

- Corticosteroid-free clinical remission at weeks 8, 14, 20 and 24.
- Need for additional medical treatment at week 14
- ≥50% reduction in faecal calprotectin by week 20 and 24
- Dietary adherence
- Quality of life

Treatment Protocol:



FC: Faecal Calprotectin, FFQ: Food frequency questionnaire, IMPACTIII: Quality of life questionnaire, 24hr/3 days: diet record.

- Phase 0 (weeks 0-2): Exclusive Enteral Nutrition (liquid diet only)
- Phase 1 (weeks 3-8): Combines partial enteral nutrition (PEN) using an enteral formula with a 6limited selection of permitted foods, while excluding processed foods, animal fats, gluten, dairy, and other pro-inflammatory or microbiota-disrupting components.

  The proportion of PEN will be determined by the research dietitian based on the patient's nutritional status. In cases of acute malnutrition, defined as a BMI < -2 SD [(26)] , or evidence of linear growth deceleration indicative of chronic undernutrition, the patient will initiate the CDED

with 50% of their daily energy requirements provided through PEN. Patients with a normal nutritional status will receive 25% of their daily energy requirements from PEN.

- Phase 2 (weeks 9–14): Gradual reintroduction of additional whole foods and continued exclusion of specific harmful dietary components.

  The proportion of PEN will be reduced by 25%; patients who initiated CDED with 50% PEN will continue with 25%, while those who started with 25% PEN will discontinue PEN altogether.

- Phase 3 (weeks 15-20): Further liberalization of the diet while continuing to avoid identified detrimental foods to support long-term remission and gut health. PEN is discontinued at this stage in all patients.

Structure of the protocol

Phase	Duration	Nordic CDED (unprocessed food)		Enteral Nutrition (liquid diet)	
		Malnutrition	Normal	Malnutrition	Normal
		% of daily energy requirements			
0	2 weeks	0	0	100%	100%
1	6 weeks	50%	75%	50%	25%
2	6 weeks	75%	100%	25%	0%
3	6 weeks	100% + 2 free days*		0%	0%

* Days that the patient is allowed to eat processed food that contains additives

At each stage of the protocol, the patient's protein requirements will be calculated to appropriately adjust the recommended intake of protein-rich, unprocessed foods.

Follow-up will continue until week 24, by which time the patient will have completed the nutritional treatment and returned to their habitual diet for 4 weeks.

Enteral Formula (liquid diet):
In line with previously published studies using CDED[16, 20, 22, 27-29], the enteral product should have certain characteristics: 1.3-1.5kcal/mL, 35-40% fat, 3,5-5g protein/100mL and no fibre. The products may include maltodextrin, soy lecithin and milk fat. To provide different flavours and consistencies 3 different brands will be chosen: Nutricia (Fortini, 2 flavours), Fresenius Kabi (Frebini Energy, 2 flavours) and Nestlé (Modulen IBD, no flavour)

Nordic CDED

The diet includes three categories: recommended, permitted, and not permitted foods (Table 1) Recommended foods: Foods that should be consumed daily to meet protein requirements and to increase the intake of starch and pectin, which benefit the gut microbiota.

Permitted foods: Includes various unprocessed foods that the patient needs to consume during treatment to ensure the diet is nutritionally complete. The list includes protein-, carbohydrate- and fat-rich foods, fruits, vegetables, herbs and spices, and beverages.

Not permitted foods: It mainly restricts the intake of ultra processed food rich in animal fat, red and processed meats, protein sources high in taurine, gluten and wheat protein, as well as food additives including maltodextrin, emulsifiers, artificial sweeteners, carrageenan, and sulphites.

It limits also the intake of fruits and vegetables containing seeds or insoluble fibres that may cause gas or abdominal pain in some patients.

Table 1. Structure of the Nordic CDED and whole foods included in each phase

	PHASE 1	PHASE 2	PHASE 3
Recommended			
Protein-rich foods	Chicken, egg, soy protein and plain yoghurt (individualised amount)		Not required
Starch-rich food	Potatoes and bananas		
Fibre-rich food	Apple, gooseberries, apricots and pear		
Allowed			
Protein-rich foods	Low fat white fish (once per week)	Addition: One can of tuna in olive oil or rapeseed oil once a week. Red meat is not recommended and should be avoided. If there is a strong desire, it should be limited to fresh, lean steak, max 200g per week (only once a week).	Addition: Other parts of the chicken, but exclude skin, wings, and offal. Fresh shellfish, lean fish, or salmon once a week (exclude pre-packaged and frozen shellfish/fish).
Carbohydrate-rich food	White rice and rice products (without additives), gluten free oats and flour (buckwheat, arrowroot, sorghum, quinoa, rice, oats and potato)	Addition: Sweet potato. Lentils, peas, chickpeas, or beans (½ - 1 cup cooked per day). Quinoa (unlimited). ½ - 1 cup rolled oats (not gluten free) 1–2 days per week.	Addition: 2 slices of bread per day (preferably homemade). A small portion of pasta (can be used instead of bread, about ½ cup cooked).
Fruits	1 avocado per day, strawberries, melon, kiwi, blueberry, raspberry and lingonberries. Allowed fruits without preservatives are fine in frozen form.	Addition: Pear, peach, cherries and kiwi. From week 10, all fruits can be introduced in small amounts, e.g., ½ dl mango, pineapple, or orange slices.	Addition: All fruits and berries including dried fruit (without sulphates), except for the non-permitted fruits/berries listed below.
Vegetables	Tomatoes, cucumber (peeled), carrot, parsnip, celeriac, pumpkin, butternut squash, fresh spinach, lettuce leaves, arugula, peas and sugar snap peas. Allowed vegetables without preservatives are fine in frozen form.	Addition: Zucchini (1 large or 2 small), 4–6 fresh mushrooms, 2 florets of broccoli or cauliflower (but not all at once). From week 10, all vegetables can be introduced in small amounts, e.g., ½ bell pepper, cabbage, and beets. Allowed vegetables without preservatives are fine in frozen form.	Addition: All vegetables except those on the non-permitted list below (provided no intestinal strictures are present).
Condiments	Oil (olive/rapeseed/avocado) and vinegar. Spices (pure): salt, pepper, paprika, cinnamon, cumin, and turmeric. Fresh herbs: mint, oregano, coriander, rosemary, sage, basil, thyme, dill, and parsley.		
Sweetener	Sweeteners: granulated sugar and maple syrup (3 tbsp/day), dark chocolate (75% cocoa) or cocoa powder.		
Beverages	Water, carbonated water, herb tea and fresh orange juice		Addition: One cup of black coffee or tea per day (avoid instant coffee and coffee capsules).

Nuts		Addition: Almonds or walnuts (unsalted, unroasted, unprocessed), 6–8 per day. Natural tahini (free from emulsifiers and sulphites), 2 tablespoons per day.
Not allowed		
Protein-rich foods	Processed, pre-cooked or smoked meat and fish. Shellfish. Red meat, pork, turkey, other parts of chicken. Other soy and dairy products. Ice cream. Plant-based milk alternatives (soy, oat, rice, or almond drinks).	
Carbohydrate-rich foods	Wheat-based products (breakfast cereals, bread, and other baked goods). Baking yeast. Gluten-free products not listed above and corn. Other soy products. Legumes (lentils, peas, chickpeas, and beans). Frozen potatoes. All other types of flour.	
Fruits	Dried fruits. All other fruits.	
Vegetables	Frozen vegetables containing preservatives. Kale, leek, asparagus, artichoke and celery. All other vegetables not listed as allowed.	
Condiments and sides	Margarine, sauces, salad dressings, corn syrup, industrially produced jam and marmalade, artificial sweeteners, mixed seasoning blends, other oils (soy oil, sunflower oil, corn oil) and oil sprays.	
Beverages:	All soft drinks, fruit juice, other sweetened beverages, alcoholic beverages, coffee, tea (except herbal tea).	
Other:	Canned products. Snacks (potato chips, pretzels, popcorn, etc.). Candy, chocolate, cakes and pastries, chewing gum.	

Treatment failure

Defined as failing to achieve a PCDAI < 15 by week-8 or any treatment changed by physician discretion besides immunomodulators (eg. biologics, corticosteroids).

Interruption of the study

In the event of unexpected complications or incidental findings of another condition, a referral will be made to an appropriate specialist in paediatric medicine or to another level of care. The need to discontinue the dietary treatment and withdraw from the study will be assessed in consultation between the physician, dietitian, and nurse. If an eating disorder is suspected or diagnosed, the patient will be referred to an eating disorder unit.

Complications: Diarrhoea (passage of 3 or more loose or liquid stools per day, or more frequent passage than is normal for the individual) or/and worsening of abdominal pain, blood in stool, vomiting, constipation (infrequent defecation, painful defecation, or both).

Data Collection:
Data will be collected from medical records and patient-reported outcomes using validated questionnaires. For the controls without nutritional treatment, the information will be taken from SWIBREG register. The REDCap system will be used as the electronic Case Report Form (eCRF).

Measurement Tools:

- **Clinical:** Paediatric Crohn's Disease Activity Index (PCDAI)
- **Anthropometric:** Weight, height, BMI (Z-score)
- **Biomarkers:** C- Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Albumin (Alb), Faecal Calprotectin (FC)
- **Dietary adherence:**
    - Web-based Food Frequency Questionnaire: SchoolMeal-Q and TeenMeal-Q [30, 31]
        - Evaluation of habitual diet (week 0) and changes in habits at the end of the study (week 24)

        - Recorded through a digital validated food frequency questionnaire accessed through a link.
    - 24-hour dietary record, 3-day food diaries.
        - Evaluation of adherence to the diet
        - 24-hour record will be done together with the dietist
        - 3- day record will be filled by the patient in a paper format.
        - Both will be analysed using Nutrition Data, a validated, web-based program for nutrition analysis and registration of diet.[32]
    - Modified MARS questionnaire and 5-point Likert scale[17]
        - Evaluation of adherence to the diet.
        - The questions will be asked and registered by the dietitian through REDCap
- **Quality of Life:** IMPACT III [33]
    - Evaluation of the patient's quality of life before, during and after the study.
    - The patient will get a link through REDCap where the answers will be filled.

Table 2: Description of the protocol

EVALUATION	SCHEDULE				
	TEN	Nordic CDED			
Phase	**0**	**1**	**2**	**3**	
WEEK	**0**	**2**	**8**	**14**	**24**
Clinical					
PCDAI [1]	X	X	X	X	X
Blood tests					
C- Reactive Protein (CRP)	X		X	X	X
Erythrocyte Sedimentation Rate (ESR)	X				
Albumin (Alb)	X		X	X	X
Fecal calprotectin (FC)	X	X	X	X	X
Anthropometric					
Weight	X		X	X	X
Length	X				X
Adherence					
24-hours food diary [3]			X	X	
3-day food diary [3]		X			
Food Frequency Questionnaire (SchoolMeal-Q, Junior Meal-Q and TeenMeal-Q) [2]	X				X
Adherence (5-point Likert Scale) [4]			X	X	X
Modified MARS [4, 5]		X	X	X	X
Quality of Life					
IMPACT III [6]	X		X		X
Personal (within routine clinical praxis)					
Doctor	X		X		X
Nurse and/or Dietist	X	X	X	X	X

[1] Journal of Pediatric Gastroenterology and Nutrition. (12): 439–447, [2] J Med Internet Res 2014;16(2) :e59, [3] Nutritiondata.se (*Front. Nutr.* 11:1395252.) [4] Inflamm Bowel Dis 2021; 27:3, [5] https://doi.org/10.1016/j.cgh.2024.12.006, [6] Acta Pædiatrica 2018 107, pp. 347–353,

Evaluation tools:

SCOFF questionnaire: A five-question screening tool designed to clarify suspicion that an eating disorder might exist. The questions can be delivered either verbally or in written form, validated in Swedish language in 2015.(25)

Food Frequency Questionnaire (SchoolMeal-Q and TeenMeal-Q): Validated interactive web-based questionnaires for assessing lifestyle factors, developed for researchers and healthcare professionals conducting research studies. SchoolMeal-Q is designed for children aged 6–10 years, and TeenMeal-Q for adolescents aged 15–18 years.(31)

Modified MARS compliance questionnaire: A questionnaire developed to evaluate compliance to the enteral nutrition and CDED diet.(1, 34)

5-point Likert Scale: A questionnaire developed to evaluate compliance to the diet therapy.(1)

IMPACT III: A valid and reliable questionnaire developed to measure health-related quality of life in Swedish children with inflammatory bowel disease.(33)

Visits

Within routine clinical praxis patients will be seen by a physician to assess disease activity (PCDAI); blood parameters (complete blood count, albumin, CRP, ESR), stool samples (FC) for clinical decision making; anthropometrics [weight (kg), height (m), BMI (kg/m^2) and Z-scores]. Baseline chemistry panel will be collected. Stool samples will be collected at each visit for FC.

Phone calls with the dietitian will be scheduled to answer patient's questions and to support dietary adherence.

The dietary intake based on a 24-hour recall and 3-day food diary will be analysed (Nutrition Data system) and specific instructions regarding the diet will be provided. The food frequency questionnaire will be answered on a web page that the patient will access through a link.

Dietary adherence will be assessed by modified MARS questionnaire and by a 5-point Likert scale ranging from highly adherence to non-adherent to the diet.

Finally, quality of life will be assessed by the IMPACT questionnaire at baseline, week 3 and 24.

A final follow-up visit will be conducted at week 24 for all patients.

Week -1, information about the study

Doctor: Review of inclusion and exclusion criteria of potential patient.

Dietitian: A recruitment phone call will be made to the parents to invite them to participate in the study. The consent forms will be sent by regular mail to be read by both parents and the patient. If the parents and the patient consent to participate in the study, samples of oral nutritional supplements will be provided for the patient to try before visit 0.

Week 0, baseline visit

Doctor: Review of inclusion and exclusion criteria. Evaluation of the severity of CD (PCDAI)

Dietitian: Description of the project and signing of the consent by both parents. Patients older than 16 years old will also sign written consent. A link to the food frequency questionnaire that should be filled before the start of EEN will be given. The patient will get on site enough enteral product to start the

introduction of EEN at home. A prescription will be made to provide with enough enteral nutrition for the coming 2 weeks. A link (REDCap) to answer the IMPACT III questionnaire will be provided.

Nurse: Anthropometric measurements (weight and length), blood (CRP, ESR, Alb) and faecal samples (FC).

Week 2

Doctor: Re-evaluation of PCDAI and medical treatment.

Nurse: Responsible to receive and send faecal sample to evaluate FC.

Dietitian: Description of Phase 1 of CDED (including written information) and prescription of enteral product for the coming 6 weeks. Information on how to fill the 3-day food record (paper form), and evaluation of adherence to TEN through modified MARS and 5-point Likert scale.

Week 8

Doctor: Re-evaluation of PCDAI, clinical assessment and medical treatment.

Nurse: Responsible for faecal and blood samples, anthropometric measurements (weight and length).

Dietitian: Description of Phase 2 of CDED and prescription of enteral product for the coming 6 weeks. Control of the previous 3-day food record and evaluation of compliance and register of adherence (5-point Likert scale).

Week 14

Doctor: Re-evaluation of PCDAI, clinical assessment and medical treatment.

Nurse: Faecal sample and blood samples, anthropometric measurements (weight and length),

Dietitian: The patient will answer a 24-hours food intake of the last day if Phase 2 (compliance evaluation) and register of adherence (5-point Likert scale). Description of Phase 3 of CDED

Week 24

Doctor: Re-evaluation of PCDAI, clinical assessment and medical treatment.

Nurse: Faecal and blood samples, anthropometric measurements (weight and length).

Dietitian: The patient will answer a 24-hours food intake recall of the last day of Phase 3 (compliance evaluation) and register of adherence (5-point Likert scale). A new link to the food frequency questionnaire will be given to evaluate changes in habitual diet after the Nordic CDED. A new evaluation of quality-of-life will be done by filling in the IMPACT III questionnaire.

Assessment of compliance:

Compliance is defined by the following parameters:

1. Intolerance: Cessation of dietary therapy due to their explicit refusal to continue following the prescribed diet regimen categorized patients as poor compliance.

2. The modified MARS questionnaire will be used to assessed adherence. Question 1 of the questionnaire - “Please indicate if you have followed the diet instructions in the way you have been asked to in the last weeks.”- The answer ‘always’ was defined as high compliance.

3. Assessment by the physician and dietitian: Compliance will be evaluated through direct questioning by physicians and dietitians. At week 8, the response of adhering to the diet ‘always’ will be categorized as indicative of high compliance. At week 14 responses of ‘always’ or ‘very often’ will be registered as high compliance. Compliance will be assessed based on per-protocol analysis.

Any other answer than ‘always’ or (‘always’ & ‘very often’) will be considered as poor compliance. To qualify as having 'high compliance,' patients need to fulfil three criteria: they need to complete the study intervention, respond with 'always' in the MARS questionnaire, and be assessed by the dietitian as 'always' at week 8, and 'always' or 'very often' at week 14.

Data analysis and statistics

- Basic demographic and clinical data will be presented as median (min–max).
- Categorical variables will be reported as frequency and percentage.

Group Comparisons: (intervention group vs. hypothesized mean or median based on historical controls):

- Numerical variables: Kolmogorov-Smirnov test or Wilcoxon Signed Rank tests
- Categorical variables: Chi-square test or Fisher’s exact test
- Friedman’s test in change over time within the intervention group

Statistical Significance:

- *A p-value ≤ 0.05 will be considered statistically significant.*

IBM SPSS Statistics software (Version 25.0, Armonk, NY: IBM Corp) will be used for analysis.

Table 3. Type of statistical analysis based on the outcome variables

Outcome variable	**Type of data**	**Statistical test** (comparisons between the intervention vs control group)	**Objective**
PRIMARY ENDPOINT			
PCDAI (week 8)	Continuous scale 0-35	Kolmogorov-Smirnov test or Wilcoxon signed-rank test	Evaluate effect between groups
PCDAI	Continuous over time	Friedman’s test (repeated measurements)	Remission over time
PCDAI	Categorical (Low, Medium, High)	Chi-Square test	Comparison of groups
Remission[1]	Yes/No	Chi-Square test	Evaluate effect between groups
SECONDARY ENDPOINTS			
PCDAI (week 14 and 24)	Continuous scale 0-35	Kolmogorov-Smirnov test or Wilcoxon signed-rank test	Evaluate effect between groups
Reduction in Faecal Calprotectin (week 24)	% of reduction	Friedman’s test	Reduction of inflammation
Faecal Calprotectin	Continuous over time	Friedman’s test (repeated measurements)	Evaluate effect in inflammation through time
Additional medical treatment (week 24)	Categorical (yes/no)	Chi-Square test	Secondary endpoint
Modified MARS questionnaire	Categorical variable (high/low compliance)	Chi-Square test or logistic regression	Evaluate adherence to the diet
R-24hr food record	Categorical variable (high/low compliance)	Chi-Square test	Evaluate compliance to the diet.
3-days food record	Continuous (energy and nutrients)	Kolmogorov-Smirnov test or Wilcoxon signed-rank test	Evaluate intake of energy and nutrients
Food frequency questionnaire	Categorical variable (healthy eating index)	Chi-Square test	Evaluate diet quality
IMPACT III	Continuous scale 0-14	Wilcoxon signed-rank test	Evaluate changes in Quality of life

1. Clinical remission: PCDAI ≤10 without systemic steroid use (expected no significant difference between the control and intervention group). Will be evaluated in week 8, 14 and 24 (% + p-value)

The statistical analysis will employ $\chi 2$ tests (or Fisher's exact test, where appropriate) for categorical variables. As we use historical controls with summarized outcome data, an appropriate one-sample test as Kolmogorov-Smirnov test or Wilcoxon Signed Rank tests will be used to compare numerical outcomes in the intervention group with hypothesized mean or medina based on control group. The changes over time with respect to continuous variables within intervention group will be conducted by Friedman's test.

Project organization

Design: 2025–2026

Recruiting. 2026–2028

Analysis and publication: 2029-2030

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