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REVIEW ARTICLE

Practical application of the Crohn's disease exclusion diet as therapy in an adult Australian population

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Abstract

There is demand from patients and clinicians to use the Crohn's disease exclusion diet (CDED) with or without partial enteral nutrition (PEN). However, the therapeutic efficacy and nutritional adequacy of this therapy are rudimentary in an adult population. This review examines the evidence for the CDED in adults with active luminal Crohn's disease and aims to provide practical guidance on the use of the CDED in Australian adults. A working group of nine inflammatory bowel disease (IBD) dietitians of DECCAN (Dietitians Crohn's and Colitis Australian Network) and an IBD gastroenterologist was established. A literature review was undertaken to examine (1) clinical indications, (2) monitoring, (3) dietary adequacy, (4) guidance for remission phase, and (5) diet reintroduction after therapy. Each diet phase was compared with Australian reference ranges for food groups and micronutrients. CDED with PEN is nutritionally adequate for adults containing sufficient energy and protein and meeting > 80% of the recommended daily intake of key micronutrients. An optimal care pathway for the clinical use of the CDED in an adult population was developed with accompanying consensus statements, clinician toolkit, and patient education brochure. Recommendations for weaning from the CDED to the Australian dietary guidelines were developed. The CDED + PEN provides an alternate partial food-based therapy for remission induction of active luminal Crohn's disease in an adult population. The CDED + PEN should be prioritized over CDED alone and prescribed by a specialist IBD dietitian. DECCAN cautions against using the maintenance diet beyond 12 weeks until further evidence becomes available.

Introduction

Whole-food dietary strategies are emerging as primary or adjunctive therapy for individuals with active Crohn's disease (CD) and offer an alternative diet therapy to exclusive enteral nutrition (EEN).[1-4] Diet is a key environmental factor implicated in the pathogenesis of inflammatory bowel disease (IBD) with a recent increased focus on the association between ultra-processed foods and the risk of developing CD and perpetuating disease course.[5,6] Although clinical trials are lacking, processed food components such as emulsifiers, thickeners, and artificial sweeteners have been shown to affect mucosal integrity, alter microbial composition, and influence intestinal barrier dysfunction in preclinical *in vitro* and animal trials.[1,7] There remains uncertainty as to how these studies translate to humans when consumed in whole foods or nutritional liquid supplements and the quantities that may cause harm. Ultimately, emerging diet therapies for active CD claim to remove these potentially deleterious food components and focus on including whole foods.[8-10]

The Crohn's disease exclusion diet (CDED) was designed more than 10 years ago as a partial food-based alternative to EEN and was initially tested as a remission induction therapy for pediatric CD.[8,11-13] More recently, in a pediatric multicenter randomized trial, the CDED supplemented with oral partial enteral nutrition (PEN) demonstrated equivalent rates of corticosteroid-free remission to EEN at 6 weeks (defined as pediatric Crohn's disease activity index ≤ 10) and superior rates of sustained clinical remission and tolerability at 12 weeks in biologic-naïve patients with ileal

involvement.[9] CDED as prescribed with PEN will be referred to as "CDED" in this paper. While CDED offers a partial food-based alternative to EEN, it remains an exclusionary diet that restricts all five core food groups and relies heavily on PEN. Briefly, the diet comprises two therapeutic phases that last 6 weeks each. Consistent between the two phases, there are five "mandatory" food items (chicken breast; eggs; peeled, cooked, and then cooled potatoes; peeled apples; and bananas) to consume daily with limited allowances of other food items. Both phases are coupled with PEN meeting 50% energy requirements in phase 1 and 25% in phase 2. The third phase is proposed as a maintenance phase following remission induction during phases 1 and 2. Evidence for phase 3 was not reported in earlier clinical trials,[9,11,12] with only one recent study reporting efficacy data beyond 12 weeks. This was a pilot study in biologic-naïve adults comparing the CDED alone with CDED and PEN over 24 weeks.[14] This pilot study demonstrated sustained clinical remission at 24 weeks in 80% of the patients who went into clinical remission at week 6 (68%). The 6-week clinical remission rates were not statistically different in those who used CDED as therapy with or without PEN (68% *vs* 57%).[14]

The evolution of the CDED as a partial food-based therapy for active CD is an exciting therapeutic option without the immunosuppressive side effects of some medical therapy. However, diet therapy is not without risk, having its own set of clinical, nutritional, and psychosocial complexities that require careful consideration to promote adherence, retain efficacy, and mitigate nutrition-related complications.[2] CDED is a prescriptive diet therapy that requires titration to disease behavior and needs to be tailored to individual nutritional requirements by a trained IBD dietitian. A detailed nutritional analysis and comparison of CDED against the Australian dietary guidelines, nutrient reference values (NRVs), and international nutrition guidelines for people living with CD has not been published. Nutritional analysis is a crucial safety component when considering the prescription of a restrictive dietary therapy especially in a nutritionally vulnerable group such as those living with IBD who have high rates of malnutrition and pre-existing restrictive eating patterns.[15,16]

Therefore, this review aims (i) to complete a comprehensive nutritional analysis of CDED with and without PEN against the Australian NRVs, the Australian dietary guidelines, and estimated nutrition requirements for patients with CD; (ii) to develop practical guidance for using CDED as therapy for adults with CD in an Australian population through consensus statements and expert opinions; and (iii) to create a clinical practice toolkit and optimal care pathway based on the above with accompanying patient and clinician resources.

Methods

A working group of nine IBD dietitians and an IBD gastroenterologist with a special interest in diet therapy for IBD was formed through Dietitians Crohn's and Colitis Australian Network (DECCAN) and Australian tertiary IBD services. All group members were experienced in using CDED and had completed the Nestle ModuLife™ CDED training module.[17]

For the consensus statements, the working group met on six occasions to discuss the clinical practicalities of using CDED as an alternative therapy to EEN. Key areas required in an optimal care pathway for standardizing the use of CDED as therapy in an Australian population while ensuring nutritional adequacy were identified. The consensus statement generation methodology was similar to that used to develop the "Exclusive enteral nutrition: Optimal care pathway for use in adult patients with active Crohn's disease."[18] The working group tasks were split into five sections to review literature on the key areas: (1) clinical indications, (2) monitoring, (3) dietary adequacy, (4) guidance for remission phase, and (5) diet reintroduction after therapy. Each group completed a literature review through large databases such as PubMed, Google Scholar, and MEDLINE with keywords of "CDED," "Crohn's Disease," and "diet therapy." Consensus statements were developed for each step in the CDED optimal care pathway and graded by hierarchy of evidence (Melnyk and Fineout-Overholt, outlined in Table S3).[19,20] Consensus was reached with $>$ 80% agreement. If there was a disagreement, available evidence and clinical experiences were discussed to form a conclusion. For the nutrient analysis, 3-day meal plans for phases 1 and 2 were created by three different dietitians, and then the average was used for analysis (Fig. S1). Meal plan portions were based on recommended daily serves from the Australian dietary guidelines.[21] Dietary adequacy of CDED was analyzed using a nutritional analysis software (Xyris FoodWorks 10© software, Brisbane, Australia).[22] For comprehensive dietary analysis, reference male and female patients were used. The reference patients were assumed to have a body mass index of 25 kg/m^2 and to be moderately physically active in line with national physical activity recommendations.[23] Nutritional prescriptions were calculated using the European Society of Parenteral and Enteral Nutrition (ESPEN) IBD guidelines for protein and energy.[15] The adequacy of macronutrients was informed by comparing with the Australian dietary guideline serve sizes for the five major food groups (fruits, vegetables, grains, dairy, and proteins).[21] The adequacy of micronutrients was informed by comparing with the Australian NRVs (recommended dietary intake [RDI] or adequate intake where RDI is not available).[24] Iron, vitamin B12, zinc, calcium, and folate are presented in the analysis, as considered the high-risk deficiencies for IBD patients as per the ESPEN IBD guidelines.[15] Adequacy was calculated as a percentage of the reference value. These data and subsequent recommendations are general in nature, and specific tailored dietary advice should be sorted from an IBD dietitian given that micronutrient requirements and nutrient risk in CD are variable and dependent on factors, including disease location, and severity, including surgical resection of the intestine, which may impair nutrient absorption, or whether appetite and oral intake are impaired during periods of active inflammation.

Additionally, a larger working party comprising DECCAN IBD dietitian members was established to develop the clinical practice toolkit. Resources including guidance on formula choice, adjusting dietary prescription for patient needs, monitoring guidance, cultural considerations, and patient resources for the adult Australian population were developed and made available for dietitians to request through the DECCAN website (https://deccanibd.org).

Results

An optimal care pathway for using CDED in Australian adults with active CD was developed to standardize the use of CDED

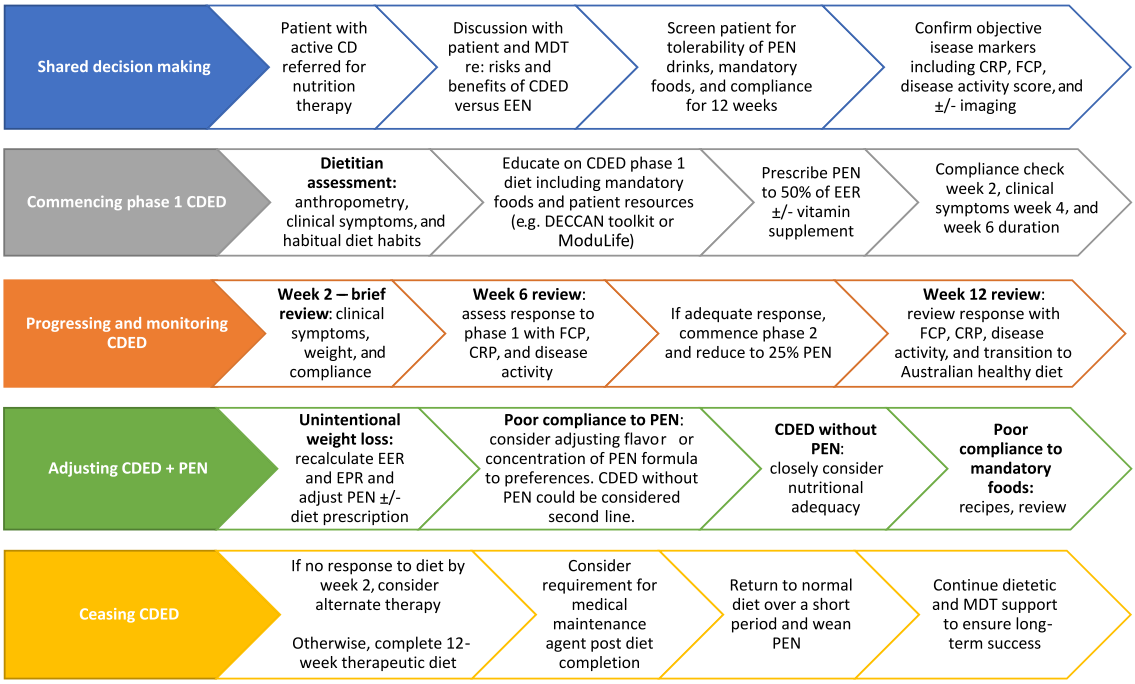

Figure 1 Optimal care pathway for implementing Crohn's disease exclusion diet (CDED) in the Australian adult population. CD, Crohn's disease; CRP, C-reactive protein; DECCAN, Dietitians Crohn's and Colitis Australian Network; EEN, exclusive enteral nutrition; EER, estimated energy requirements; EPR, estimated protein requirements; FCP, fecal calprotectin; MDT, multidisciplinary team; PEN, partial enteral nutrition.

and guide its practical application and monitoring when using CDED as therapy (Fig. 1).

Consensus statements. Below, we present five key consensus statements and the evidence supporting these statements.

1. When to use CDED as a primary or adjunctive therapy for active CD

Clinical indications for CDED + PEN therapy in adults with active luminal CD

CDED phases 1 and 2 may be considered as an alternative to EEN and may be as effective as EEN and corticosteroids for remission induction in adults with mild to moderate luminal CD. (IV)

1.1 Remission induction

Current data derived from a pediatric randomized controlled trial (RCT) and retrospective case series including adult patients support the role of CDED + PEN for induction of clinical remission.[9,14] While symptoms and clinical disease activity scores were observed to improve in current studies, there is a lack of endoscopic data, and it is well recognized that symptoms do not always reflect mucosal or histological amelioration of inflammation in CD. The seminal pediatric RCT compared CDED with an EEN group, the latter transitioning to an unrestricted diet at week 7 with a primary endpoint of diet tolerance at week 12.[9] The study described promising signs of decreased inflammatory markers by week 6 such as a reduction in median fecal calprotectin in both groups (CDED, $P = 0.002$; EEN, $P = 0.01$), but there was no statistically significant difference between the groups ($P = 0.43$).[9] By week 12, biochemical remission (defined as fecal calprotectin < 50 and C-reactive protein [CRP] < 5) was not achieved on either diet. A greater proportion of participants in the CDED arm had sustained normal CRP and corticosteroid-free remission (CDED phase 2 = 28/37 [75.6%] *vs* EEN unrestricted/free diet group = 13/31 [45.1%], $P = 0.01$); however, the EEN group was not on any therapy between weeks 6 and 12 as they had returned their habitual diet.[9] In the more recent open-label pilot randomized trial in adults with mild–moderate CD, patients were assigned to either CDED + PEN or CDED alone, with no true control group. Beyond some noted dropout (hinting to tolerance), moderate rates of remission were seen at week 6, with 68% in CDED + PEN and 57% in CDED alone, without significant difference between the groups ($P = 0.46$).[14] This is the first presented diet therapy with endoscopic endpoints where a small subgroup (14/40 of which 8 received CDED and 6 CDED without PEN) achieved endoscopic remission.[14] Further work needs to be completed to establish the endoscopic, radiological, and histological effects of CDED ± PEN, in keeping with the modern treat-to-target paradigm.

As with any therapeutic intervention, compliance is crucial to increased efficacy. Adult's compliance to CDED alone was 86% and with PEN 63%,[14] which are both comparable with adult's compliance to EEN ranging from 60% to 80% depending on the center.[25,26] By drawing on EEN data and extrapolating CDED to

adults with CD, it seems reasonable to propose that CDED can induce clinical remission of mild to moderate luminal disease; however, further evidence of objective amelioration of mucosal inflammation is required. It must also be noted that the clinical trials of CDED only included biologic-naïve patients with ileal involvement and that the observational study in pediatric patients failing biologics, including some with isolated colonic disease, reported very small numbers entering clinical remission (three of six patients).[12]

Given that some solid foods permitted alongside PEN in CDED, it is expected that the diet may be better tolerated than EEN, particularly in adults, especially as tolerance of the liquid diet and dropout is a limitation of EEN.[27] A patient's disease state, location,[27] diet therapy preference, tolerance, and lifestyle factors should be considered in deciding between EEN and CDED, while being mindful that EEN has a greater depth of evidence behind it.

The evidence base for EEN is well established across age groups and disease types and, particularly, as first-line therapy in pediatric cohorts.[28-30] Therefore, EEN should not be overlooked. EEN leads to rapid response (2–6 weeks), induction of mucosal healing, and improvement of nutritional status.[28,29,31] EEN is considered an effective alternative to corticosteroids,[29,30,32] while also being an effective salvage therapy for anti-tumor necrosis factor alpha.[29,30,33]

1.2 Managing complications and optimization/avoidance of surgery

There is currently no evidence to support either the role of CDED in managing complications of CD or optimization before surgery. Phases 1 and 2 of CDED meet total daily fiber requirements (predominately soluble fiber in phase 1) and may be tolerated by patients with symptomatic stricturing disease; however, evidence to support safety of insoluble fiber (particularly in phase 2) for patients with symptomatic strictures is not available. By comparison, some studies have shown that EEN may be effective for the management of CD-related complications,[34] with evidence that EEN can lead to radiological resolution of stricturing disease,[35] healing of enterocutaneous fistulae,[34,35] improved health related quality of life[36] and reduction of theater time, complications, and need for stomas.[36-39] EEN may even lead to surgical avoidance altogether, with small observational studies showing that presurgical optimization with EEN mitigated the need for surgery and allowed successful bridging to immunomodulator therapy.[39] Of note, the CDED has been piloted in patients with chronic pouchitis,[40] and the published results of planned control trials are anticipated.[40]

1.3 Real-world application of therapeutic diets

Crohn's disease exclusion diet may be proposed as an alternative for adults with CD who do not tolerate EEN as it does provide the freedom to eat some solid foods that may appeal to some patients. Additionally, while there is no published evidence, there is consensus among DECCAN IBD dietitians that CDED could be used as a weaning strategy following a therapeutic time of EEN for remission induction given the high relapse rates post EEN cessations.[41] This may offer a prolonged and supportive duration of efficacy.

To date, there is no published evidence regarding cyclic use of CDED as induction for future flares. However, patients who are successful with initial CDED remission induction may also consider additional short-term CDED as treatment for future flares as has been done with EEN previously. This approach could also be used as an alternative to steroids or EEN where appropriate.

2. Clinical response and monitoring of active luminal CD to CDED + PEN

Clinical monitoring of CDED + PEN

Two weeks of the CDED + PEN may be adequate to determine response to the diet. (II)

Careful monitoring of patients on the CDED diet is recommended. (VII)

2.1 Clinical response and monitoring

A secondary multivariable analysis of the pediatric RCT showed that remission at week 3 was associated with ongoing remission at week 12.[9] In patients on EEN, disease activity and biomarkers display response after 2 weeks[42]; therefore, similar should be expected in CDED. Local practice for clinical monitoring frequency should be adapted to CDED. At a minimum, clinical response was assessed at the end of week 2, and biomarkers were reviewed at the end of week 6. A guide for monitoring schedule is outlined in this optimal care pathway (Fig. 1).

Interpretation of clinical response in practice may be guided by improvement in clinical disease activity including Crohn's disease activity index or the Harvey–Bradshaw index coupled with objective inflammatory biomarkers CRP and fecal calprotectin.[43,44] If response is not achieved after 2 weeks of therapy, it may be appropriate to cease CDED and consider an alternative, such as EEN, or conventional medical therapy, such as corticosteroids. Clinical response and remission should be discussed with multidisciplinary team and patient.

2.2 Monitoring dietary prescription and compliance

Careful monitoring of patients by an IBD dietitian trained in the use of the CDED is recommended to monitor for nutritional adequacy, dietary compliance, and nutrition status. Diet recall and/or the CDED compliance checklist[9] can be utilized to ensure the patient is compliant with both PEN and mandatory foods. Appetite, fatigue, and weight should be used to monitor adequacy of dietary prescription and to inform adjustments.

2.3 Patient education

Education on dietary therapy, compliance, and adjustments should be completed by (or in consultation with) a specialist IBD dietitian. Both the DECCAN[45] and ModuLife™[19] education resources support compliance with additions such as meal plans and recipes. IBD dietitians will evaluate the restrictive nature of CDED and appropriateness for patients exhibiting signs of disordered eating risk or food fear.

3. Nutritional monitoring and adjusting CDED nutritional prescription

Nutritional monitoring of CDED

Nutrition adequacy of the CDED should be carefully considered and prescription adjusted to patient needs by an IBD dietitian. (VII)

Supplement with calcium, particularly in phase 2 of the diet, when unable to meet requirements with PEN formula. (VII)

3.1 Evaluating the nutritional adequacy of CDED

The nutritional adequacy of CDED with and without PEN is outlined in Tables S1A and S1B. Overall, the CDED is nutritionally adequate for Australian reference adult patients across a number of macronutrients and micronutrients. Minor nutritional deficits over a monitored 12-week period pose low clinical risk, but longer-term restriction increases the risk of nutrient deficiencies and associated complications.

3.2 Energy provision

The following phases are from the dietitian-designed meal plans:

Phase 1 food components provide ~50% of energy requirements with a reasonable volume of food. The "allowed" foods add variety, fiber, and additional energy, vitamins, and minerals.

Phase 2 food components provide ~60–68% of energy requirements. PEN prescription is recommended to supplement 25% of energy; therefore, the example food components of phase 2 provide insufficient energy, shy of the 75% prescribed.

In both phases, close monitoring for signs of an energy deficit is recommended (e.g. weight loss and fatigue) with encouragement to eat sufficient "allowed" foods to meet energy demands. Alternatively, PEN could be increased.

Phase 3 food components were not analyzed in this review, as long-term adherence to phase 3 of the diet is not recommended (see section 5.1).

An IBD dietitian should guide personalization of the CDED nutritional prescription. For example, those from a culturally diverse background may require additional support in adapting the diet to cultural preferences. Further suggestions for adjusting diet prescription are outlined in the accompanying CDED toolkit[45] and section 3.8.

3.3 Protein

The CDED is exceedingly high in protein across all phases. The ESPEN guidelines propose that patients with active IBD require between 1.2 and 1.5 g of protein/kg body weight/day. While this range is based on poor-quality data, the upper recommendation was used to demonstrate a highly catabolic IBD patient.[15] Nonetheless, phases 1 and 2 of the CDED exceed these recommendations, providing 125% of protein requirements for a catabolic patient (up to 1.8 g of protein/kg body weight/day) and 195% of protein requirements for patients with a more normal nitrogen balance (1 g of protein/kg body weight/day). For those patients in remission or healthy controls, CDED would provide approximately two and a half times their required daily protein.[15] Protein intakes should be tailored and monitored, particularly for patients who may already be malnourished, have significant malabsorption, be aiming for weight gain, or have increased protein needs due to other comorbidities such as obesity. Caution should be taken with excess protein, particularly in those with colonic disease, with the risk of distal protein fermentation.[2]

3.4 Fiber

Phases 1 and 2 of the diet meet 80–100% of recommended fiber intake for our reference patients, dependent on fibrous food choices from the "allowed foods" list. While adequate fiber intake was possible based on the dietitian-designed meal plans, it is recognized in clinical practice that IBD patients often do not eat enough fiber.[46] An IBD dietitian can advise on optimizing different fibers to ensure adequacy during CDED.

3.5 Food groups

In Table S2, the meal plans are compared with the recommended intake of food groups according to the Australian Guide to Healthy Eating. Key findings include inadequate provision of whole grains, dairy foods (phase 2), and no plant-based proteins. There is, however, inclusion of healthy fats with olive oil and avocado.

3.6 Micronutrients

The CDED meets > 80% of the key micronutrients' RDI/adequate intake for the reference patient, with the exception of calcium in phase 2, which is significantly decreased with the reduction of PEN prescription.

Inflammatory bowel disease dietitians should compare the calcium content of the patient's PEN prescription to the patient's requirements and advise weather calcium supplementation is required. Patients at high risk of nutrient deficiency should undergo micronutrient screening as per the ESPEN IBD guidelines,[15] but caution should be used to interpret results during periods of acute inflammation.[47]

See section 4 for considerations without PEN. The inadequacy of the diet components is of particular concern for "phase 3" of the diet, which does not include PEN and is not recommended to follow long term.

It is acknowledged that patients with IBD are at higher risk of micronutrient deficiencies, with intestinal inflammation and surgeries limiting absorptive capacity.[47,48] Inflammation itself also makes interpretation of micronutrient results challenging, as many are acute-phase reactants. IBD dietitian review and personalized supplementation is recommended.

3.7 Omega 3 fatty acids

Omega 3 fatty acids were included in the analysis because of their anti-inflammatory properties. Only avocado and the weekly tuna allowed in phase 2 are good sources of omega 3s. There are no data on the omega 3 content of the nutrition supplements utilized for this analysis, but the reported omega 6:3 ratio is 5.1:1, which is within the recommended range.[24]

Table 1 Restriction or exclusion of food-based dietary components within the Crohn's disease exclusion diet and Australian recommendations for reintroduction at the end of phase 2 (week 12)

Food component	Phase 1	Phase 2	Phase 3	General evidence for long-term exclusion of food components for patients with CD	Evidence quality	Recommendations for after phase 2 (week 12)	Benefits of food component/nutrient
Dairy	†	†		• ONS in EEN and PEN of CDED are dairy based (whey protein) yet induce remission.[49] • Exclusion of lactose may be indicated rather than cow's milk protein. • No association between dairy consumption and developing CD.[50]	Low	Reintroduce dairy in phase 3. Use lactose-free if intolerance suspected.	Calcium B12 Protein
Gluten				• It is theorized gluten or its associated wheat-protein components (e.g. amylase trypsin inhibitor) promote intestinal inflammation via altered small intestinal immune activation. • Gluten has only been examined in cross-sectional surveys of self-reported gluten sensitivity in patients with IBD[51,52] without objective markers of disease improvement. • No RCTs exist to confirm or negate its role.	Low	Liberalize wholegrain gluten-containing foods (e.g. wheat, barley, rye, and oats) in line with Australian dietary guidelines.	Wholegrain Fiber B vitamins Prebiotics
Red and processed meat		‡		• No evidence to support restricting red meat in CD patients. • A key prospective RCT compared high *versus* low levels of consumption of red meat and processed meat in CD saw no difference in relapse rates between the two intervention groups.[53]	Low	Include lean red meat, poultry, eggs, fish, pork, and plant-based proteins. Limit processed meat in line with the Australian dietary guidelines.[21]	Iron B12 Zinc Protein
Ultra-processed foods (UPF)				• Inconclusive evidence to recommend restrictions of UPF. • Systemic reviews of four large cohort studies suggest that UPF are positively associated with risk of CD.[54] • Preclinical data suggest specific emulsifiers and thickeners including maltodextrin, yet mechanisms and translation to human diets remain unclear as published human clinical trials are lacking.[55] • PEN and EEN contain these food additives yet induce endoscopic remission.[7,48,49] • No evidence for avoiding sulfite preservatives or microparticles.[56,57]	Emerging	Minimize intake of discretionary items to 0–2 serves per day in line with the Australian dietary guidelines.	Limited nutritional benefit to discretionary UPF

(Continues)

Food component	Phase 1	Phase 2	Phase 3	General evidence for long-term exclusion of food components for patients with CD	Evidence quality	Recommendations for after phase 2 (week 12)	Benefits of food component/nutrient
Fiber	Limited	[§]	Increased	• All CDED phases contain ~25 g/day fiber from allowed foods (above parameters of a low-fiber diet [10–15 g/day],[58] and median population intakes). • There is minimal evidence for a low-fiber diet utility in CD.[58] A low-fiber intake has been associated with an increased risk of flare, and habitually, individuals with CD have inadequate fiber intakes.[59] • No studies have been conducted examining tolerability of diets high in fermentable fiber in patients with active CD. • No prescriptive targets for resistant starch and pectin; however, intake is recommended.[60]	Low	Recommendation: liberalization of a broad variety of fiber-containing foods in line with the Australian Guide to Healthy Eating.[21]	In line with the healthy population, there are global health benefits of good fiber intake. This includes, but is not limited to, heart health, cholesterol management, and gut microbiota diversity

[†]Cow's milk protein in PEN.
[‡]Weekly red meat allowed but discouraged.
[§]Increased fruit, vegetables, quinoa, and nuts.
CD, Crohn's disease; CDED, Crohn's disease exclusion diet; EEN, exclusive enteral nutrition; IBD, inflammatory bowel disease; PEN, partial enteral nutrition; RCT, randomized controlled trial.
Key: Avoidance Limited Increased

3.8 Adjustments to mandatory components

The CDED has not been clinically tested without any of the mandatory foods. As such, clinicians cannot say with certainty whether a modified version of the diet will be efficacious. The therapeutic benefit of individual dietary components has not been clearly elucidated in human trials, leaving the possibility that the removal of deleterious foods leads to the success of the diet.

In practice, those who are vegan, vegetarian, or have food intolerances may want to remove one or more of the mandatory food components. Clinical reasoning and pragmatics should always be considered; that is, if the CDED is deemed the most appropriate or only accepted therapy by the patient, an adjusted CDED implemented within a defined timeframe may offer some therapeutic benefit over nil therapy. Macronutrient and micronutrient adequacy should be evaluated. Further commentary is available in the DECCAN CDED clinical practice toolkit. We do not recommend the use of fruit-based oral supplement drinks because all clinical trials use dairy-based PEN and fruit-based supplements are not nutritionally complete.[49]

4. Nutritional adequacy, safety, and efficacy of CDED without PEN

Using CDED without PEN
CDED without PEN is not yet recommended due to nutritional inadequacy and limited evidence. (VII)

Crohn's disease exclusion diet alone compared with CDED + PEN has been piloted in an RCT of 44 biologic-naïve adult CD patients with mild to moderate disease.[14] Clinical remission as defined by the Harvey–Bradshaw index was achieved at week 6 and sustained at week 24 in a larger proportion of those in the CDED + PEN group (n = 12) compared with CDED alone (n = 8).[14] Thirty-five percent of the total group (14 of 40 patients) reached endoscopic remission at 24 weeks,[14] of which 8 (57%) were CDED + PEN and 6 (42%) CDED alone. An appropriately powered RCT is anticipated to validate these pilot findings.

At this stage, CDED without PEN is not recommended due to its restrictive nature and subsequent risk of micronutrient deficiencies. As outlined in Tables S1A and S1B, consumption of reasonable quantities of mandatory and allowed foods during phases 1 and 2 of CDED (without PEN) leads to diet that is inadequate in energy, zinc, and calcium for men and women and inadequate also in iron for women. The mandatory foods alone are inadequate in all micronutrients; therefore, consumption of daily "allowed foods" and PEN are critical for CDED to be nutritionally adequate.

5. Weaning CDED towards the Australian dietary guidelines

CDED maintenance diet and dietary reintroduction
Phase 3 is currently not recommended as a long-term maintenance diet. (VII)

Table 2 Recommendations from Dietitians Crohn's and Colitis Australian Network (DECCAN) for reintroducing diet after phase 2 (week 12) of the Crohn's disease exclusion diet

Approaches to consider	Description	Presenting patient	Practical application
Recommended			
Based on expert opinion, returning to a well-balanced, liberalized habitual diet with education towards the Australian Guide to Healthy Eating, guided by an IBD dietitian			
"Rapid" reintroduction	Transition to the Australian Guide to Healthy Eating over 5–14 days.	• Struggling with adherence • Upcoming social events	• Reintroduce 1 meal per day, and then introduce snacks after day 3 • Wean PEN with introduction of snacks (unless clinically indicated, i.e. pre-existing malnutrition or aiming for weight gain) • Counsel on general healthy eating principles • IBD dietetic review after diet reintroduction
Introducing "free days"	Transition to two "free" days and five CDED days.[17] Wean CDED principles over 4–6 weeks to resume habitual diet.	• Apprehensive about diet reintroduction • Upcoming social events There is no published evidence to support this approach	• Two "free days" may include a meal in a restaurant, or favorite snack foods and desserts • ± PEN pending patient compliance and nutrition goals • Longer term could consider increasing to 3–4 "free days" • IBD dietetic review may be required more frequently to guide and support through this stage
Not recommended			
Continuing phase 1 or 2 of CDED	Long-term use of CDED phase 1 or 2 beyond 12 weeks.	• Apprehensive about risk of flare • Wanting to sustain response using diet • Not on a maintenance therapy • Awaiting a change in medical therapy	• Counsel on dietary adequacy, variety, and psychosocial risks of a restricted diet • Counsel towards "free days" as above • Educate on general IBD diet principles in line with Table 1 (see appendices in CDED toolkit for education sheets) • Frequent dietetic monitoring and review • Review need for ongoing PEN at 25% of nutrition requirements but caution impact of taste fatigue on future EEN therapy • Calcium supplement and/or multivitamin for dietary adequacy

CDED, Crohn's disease exclusion diet; EEN, exclusive enteral nutrition; IBD, inflammatory bowel disease; PEN, partial enteral nutrition.

5.1 Review of diet component restrictions in CDED and mechanisms of action

The mechanism of action of CDED remains ambiguous with justification for inclusion and exclusion of foods or food groups largely relying on preclinical data, leaving clinicians uncertain of how individualizing components may affect the diets' efficacy in humans. The diet is high in protein and iron with good fiber content; it contains potentially "deleterious" food additive and its overall nutritional composition is more similar to EEN than to a whole-food diet. Individual dietary components and their evidence for inclusion or exclusion are explored in Table 1.

Of note, while individual nutritional components may be considered as "beneficial" or "harmful," the CDED diet as a whole may confer different "synergistic" physiological effects than the individual nutrients/food components. Further research is required to clarify which components of the diet are contributing to its efficacy and impacting the gut microbiota and systemic inflammation, which may allow a more liberal diet for longer-term use.

5.2 Diet reintroduction

There is currently limited evidence to support phase 3 of the CDED with no RCT published on this phase to date. The diet phase is low in wholegrains and dairy when compared with national guidelines. Further, long-term restriction imposed by phase 3 may increase risk of malnutrition, disordered eating, poor food-related quality of life, and mood disorders and depression, for which diet is now thought to have a role in preventing and managing.[59,61–63] Given the concerns outlined, we currently cannot support the dietary restrictions imposed by the CDED phase 3 long term.

There is limited guidance on the pace for reintroduction and what constitutes a regular diet and after CDED diet therapy; therefore, clinical practice guidance for the Australian population was developed on expert experience and consensus. Some approaches and considerations are outlined in Table 2.

Conclusion

The CDED provides a promising alternative to EEN and corticosteroid therapy for the adult CD population. Caution should be taken when drawing parallels between first-line EEN therapy and the emerging body of evidence of the CDED. There are many factors to consider when prescribing the CDED to adult patients including nutritional adequacy, nutrition status and goals, optimal monitoring, patient preference, tolerability, compliance, dietary reintroduction, and risk of continuing unnecessary dietary restrictions. CDED should be prescribed and monitored with a multidisciplinary team including an IBD dietitian.

Without current publication of sufficient studies outlining the use of the CDED longer term, DECCAN does not recommend prolonged adherence to the CDED beyond 12 weeks. Pace of dietary reintroduction should be patient centered and supported by an IBD dietitian. There is no evidence for long-term restriction of any dietary components.

Areas for future research include use of CDED for optimization before surgery, as a bridging therapy pending therapeutic efficacy of conventional therapy, as a bridge from EEN therapy, and CDED without PEN. Outcomes should also consider real-time dietary adequacy, adherence, and patient-reported outcomes such as quality of life, diet satisfaction, and disordered eating behaviors.

While this partial food-based diet offers a promising alternative to EEN and corticosteroids to induce disease remission in CD, further research into CDED phase 3 for maintenance therapy is required. By analyzing nutritional adequacy in all phases of the diet and exploring the intraluminal mechanistic action of restricted foods and dietary components, we hope to minimize unnecessary dietary restriction in a patient group already vulnerable to food avoidance, malnutrition, poor food-related quality of life, disordered eating, and micronutrient deficiencies.

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Data availability statement. The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1: Crohn's Disease Exclusion Diet Phase 1 and 2 example meal plans developed by IBD dietitians and used for dietary analysis.

Table S1A: Nutrient analysis of Crohn's Disease Exclusion Diet example meal plans- Male.

Table S1B: Nutrient analysis of Crohn's Disease Exclusion Diet example meal plans- Female.

Table S2: Crohn's Disease Exclusion Diet Phase 1 and 2 meal plans compared to the Australian Dietary Guidelines daily food group intake recommendations.

Table S3: Hierarchy of evidence - Melynyk and Fineout-Overholt (20).