THE OFFICIAL JOURNAL OF THE BRITISH DIETETIC ASSOCIATION

Journal of Human Nutrition and Dietetics

Journal of Human Nutrition and Dietetics

CLINICAL NUTRITION

British Dietetic Association evidence-based guidelines for the dietary management of Crohn's disease in adults

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Keywords
Crohn's disease, diet, dietary fibre, enteral nutrition, exclusion diet, food re-introduction diets, prebiotics, probiotics, strictures.

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How to cite this article
Lee J., Allen R., Ashley S., Becker S., Cummins P., Gbadamosi A., Gooding O., Huston J., Le Couteur J., O'Sullivan D., Wilson S., Lomer M.C.E. & on behalf of Gastroenterology Specialist Group of the British Dietetic Association. (2014) British Dietetic Association evidence-based guidelines for the dietary management of Crohn's disease in adults. *J Hum Nutr Diet.* **27**, 207–218
doi:10.1111/jhn.12176

Abstract

Background: Crohn's disease is a debilitating chronic inflammatory bowel disease. Appropriate use of diet and nutritional therapy is integral to the overall management strategy of Crohn's disease. The aim was to develop evidence-based guidelines on the dietary management of Crohn's disease in adults.

Methods: Questions relating to the dietary management of Crohn's disease were developed. These included the roles of enteral nutrition to induce remission, food re-introduction diets to structure food re-introduction and maintain remission, and dietary management of stricturing disease, as well as whether probiotics or prebiotics induce or maintain remission. A comprehensive literature search was conducted and relevant studies from January 1985 to November 2009 were identified using the electronic database search engines CINAHL, Cochrane Library, EMBASE, MEDLINE, Scopus and Web of Science. Evidence statements, recommendations, practical considerations and research recommendations were developed.

Results: Fifteen research papers were critically appraised and the evidence formed the basis of these guidelines. Although corticosteroids appear to be more effective, enteral nutrition (elemental or non-elemental) can be offered as an alternative option to induce disease remission. After a course of enteral nutrition, food re-introduction diets may be useful to structure food re-introduction and help maintain disease remission. Dietary fibre is contraindicated in the presence of strictures as a result of the risk of mechanical obstruction. The use of probiotics and prebiotics is not currently supported.

Conclusions: As an alternative to corticosteroids, evidence supports enteral nutrition to induce disease remission. Food re-introduction diets provide structure to food re-introduction and help maintain disease remission. These guidelines aim to reduce variation in clinical practice.

Introduction

Crohn's disease is a debilitating chronic inflammatory bowel disease (IBD) with no known cure. It is characterised by patchy, transmural inflammation and ulceration affecting anywhere in the gastrointestinal tract, with ileocolonic disease being the most frequent presentation (Sands, 2004). The cause is not fully understood, although it involves a genetic predisposition, environmental risk factors and immune dysfunction (Ardizzone & Bianchi, 2002; Bernstein *et al.*, 2010). It most commonly presents in adolescents and young adults and its prevalence is equal among men and women (Loftus, 2004) and varies across the world. The reported highest annual incidence of Crohn's disease for Europe, Asia (including the Middle East) and North America are 12.7, 5.0 and 20.2 per 100 000 person-years, respectively (Molodecky *et al.*, 2012). Prevalence data for Europe and North America are 322 and 319 per 100 000 persons, respectively (Molodecky *et al.*, 2012). Crohn's disease affects 87 000 people in the UK (Mowat *et al.*, 2011) with between 3000 and 6000 new UK cases being diagnosed each year (Loftus, 2004).

Crohn's disease follows an unpredictable relapsing and remitting time course with acute flare-ups of disease interspersed with periods of remission. Symptoms include abdominal pain, diarrhoea, urgency of defecation, fatigue and anaemia. Malnutrition and weight loss are common, occurring in up to 85% of patients (Gassull & Cabre, 2001; Nguyen *et al.*, 2008; Gerasimidis *et al.*, 2011).

Primary treatment aims are to induce and maintain remission and prevent disease progression. Management options include drug therapy, surgery and enteral nutrition. Corticosteroids, aminosalicylates, immunosuppressive drugs and, more recently, biological agents (e.g. anti-tumour necrosis factor) are the mainstay of medical management and many patients have surgery (Bernstein *et al.*, 2010; Dignass *et al.*, 2010).

The expertise of a registered dietitian is vital in the dietary and nutritional management of Crohn's disease (IBD Standards Working Group, 2009; Lomer, 2011) and advice on diet is one of the most pertinent issues for people with Crohn's disease (Prince *et al.*, 2011). Patients often alter their dietary intake with negative impact on nutritional status. Published guidelines for the diagnosis and management of Crohn's disease are available (Bernstein *et al.*, 2010; Dignass *et al.*, 2010; Van Assche *et al.*, 2010; Mowat *et al.*, 2011) and include some information on diet, although they are not sufficiently detailed to offer comprehensive practical guidance; thus, dietetic guidelines are required to support and improve the clinical services that patients receive (Lomer, 2009). The aim of these guidelines is to systematically review key aspects of the dietary management of Crohn's disease in adults to provide evidence-based guidelines.

Materials and methods

A Crohn's disease Dietetic Guideline Development Group (Crohn's-DGDG) was formed comprising registered dietitians belonging to the Gastroenterology Specialist Group of The British Dietetic Association (BDA). Four key topic areas and associated questions were devised based on research literature, clinical practice, emerging evidence and gaps in the Crohn's disease evidence base associated with diet (Table 1). Where evidence was not available, to ensure that the guidelines would be comprehensive and practical from the point of contact with the dietitian, the Crohn's-DGDG generated some general guidance for dietetic service provision and clinical and dietary assessment through consensus of current practice and, where possible, evidence from the literature (Lewis & Scott, 2007; UK IBD Audit Steering Group, 2007, 2009; IBD Standards Working Group, 2009; Bernstein *et al.*, 2010; Dignass *et al.*, 2010; Van Assche *et al.*, 2010; Mowat *et al.*, 2011). The evidence for dietetic service provision and clinical and dietary assessment was not formally reviewed and is described in the full BDA guidelines (see Supporting information, Data S1).

For each question, inclusion criteria were identified relating to participants, interventions, comparisons, outcome measures and types of study (PICOT). Relevant studies were assessed against these criteria. Generic inclusion and exclusion criteria were set for participants and type of studies, and interventions, comparisons and outcome measures were topic specific (Table 2; for further details for PICOT for each question, see Supporting information, Data S1).

A comprehensive literature search was conducted and relevant studies from January 1985 to November 2009

Table 1 Topics and questions specific to guideline

As a treatment to induce remission:
Is exclusive enteral nutrition as effective as corticosteroids?
Is elemental or non-elemental enteral nutrition more effective?
After induction of remission by nutritional means:
Are food re-introduction diets effective for maintaining remission?
Which type of food re-introduction diet is most effective for maintaining remission?
In stricturing disease, does decreasing dietary fibre (residue) reduce:
The risk of bowel obstruction?
Self-reported gastrointestinal symptoms?
Do probiotics or prebiotics:
Induce remission?
Maintain remission?

Table 2 Inclusion and exclusion criteria

Criteria	Inclusion criteria	
Participants	Adults (18 years or older) except where indicated Crohn's disease diagnosed by standard methods (e.g. histological and/or radiological findings) No co-existing gastrointestinal disease or pregnancy*	
Interventions	Topic specific	
Comparison	Intervention compared to placebo, no treatment, usual diet, other dietary component or corticosteroids	
Outcome measures	Enteral nutrition	Remission assessed in terms of remission rates and defined by standard methods (e.g. histological and/or radiological findings or disease activity index) in the same way in the intervention and comparison groups Maintenance of remission assessed in terms of remission or relapse rates and defined by standard methods (e.g. histological and/or radiological findings or disease activity index) in the same way in the intervention and comparison groups
	Food re-introduction diet	Maintenance of remission assessed in terms of remission or relapse rates and defined by standard methods (e.g. histological and/or radiological findings or disease activity index) in the same way in the intervention and comparison groups
	Strictures	Bowel obstruction Participant reported bowel symptoms assessed on an objective scale
	Probiotics and prebiotics	Remission assessed in terms of remission rates and defined by standard methods (e.g. histological and/or radiological findings or disease activity index) in the same way in the intervention and comparison groups Maintenance of remission assessed in terms of remission or relapse rates and defined by standard methods (e.g. histological and/or radiological findings or disease activity index) in the same way in the intervention and comparison groups
Types of studies	Intervention studies comparing the intervention diet to placebo, no treatment or another dietary component Nonsystematic reviews, case studies, retrospective audits or studies in abstract form only were excluded	

*As a result of limited methodological reporting in some of the studies, the Crohn's disease Dietetic Guideline Development Group agreed to include studies where co-existing gastrointestinal disease or pregnancy were not described.

were identified using the electronic database search engines CINAHL, Cochrane Library, EMBASE, MEDLINE, Scopus and Web of Science. At the outset, studies before 1985 were excluded because of differences in other aspects of medical, surgical and dietary management that make comparisons with current practice difficult. Searches were restricted to identify studies in humans, adults and the English language (for search terms, see Supporting information, Data S1).

Relevant studies were identified using the title and abstract. Reference lists of applicable studies were also cross-searched for other studies of potential relevance. Relevant studies already known to the Crohn's-DGDG but which had not been identified by the literature searches were also included for evaluation.

For each question, at least two members and the lead (JL) of the Crohn's-DGDG independently assessed the relevant studies using the Scottish Intercollegiate Guidelines Network (SIGN) appraisal tools (SIGN, 2008). After quality assessment and consensus agreement, each study was assigned a level of evidence using the SIGN criteria. SIGN methodology recommends the exclusion of studies assigned a negative level of evidence indicating a study of poor methodological quality. However, as a result of the limited availability of evidence for these guidelines, the Crohn's-DGDG agreed to include studies that were assigned a negative level of evidence and to consider the lower methodological quality when formulating and grading the recommendations.

Considered judgement was formulated using standard levels of evidence and grading of recommendations (SIGN, 2008). Consensus agreement of the evidence was achieved by round table discussion within the Crohn's-DGDG with development of evidence statements, recommendations for dietetic practice including practical considerations and research recommendations. Where evidence was lacking, no recommendation was made but practical considerations were provided. At least eight members of the Crohn's-DGDG were present at each meeting. Members who were unable to attend a meeting were given the opportunity to contribute before and after each meeting. The terms 'limited' or 'moderate' and 'weak' or 'good' were used to describe the volume and quality of evidence, respectively.

A consultation draft of the guidelines were peer reviewed by twenty-three gastroenterologists, IBD clinical nurse specialists, registered dietitians, researchers and patients. The final guidelines were peer reviewed and ratified by the BDA Professional Practice Board.

Results

The literature search identified 809 potential papers to review. However, the majority (n = 756) did not address

Table 3 Clinical practice recommendations

Clinical practice recommendation	Grade of recommendation
Enteral nutrition	
Although medical therapy is the mainstay of treatment for active Crohn's disease, enteral nutrition can be offered as an alternative primary treatment to induce clinical remission	C
When enteral nutrition is used for induction of clinical remission:	C
Elemental, semi elemental or polymeric formulas can be used	
The formula can be given orally or via an enteral feeding tube	
It can be achieved between 10 days and 6 weeks	
Food re-introduction diets	
After induction of remission by nutritional means, food re-introduction diets such as an elimination or LOFFLEX diet can be considered as a starting point for food introduction and may be helpful for maintenance of remission	C
High-fibre diets are not indicated as food re-introduction diets.	D
Dietary fibre in stricturing disease	
Insufficient evidence to support a recommendation	–
Probiotics and prebiotics	
Using probiotics to induce or maintain remission in Crohn's disease is not currently supported.	B

LOFFLEX, low-fat fibre limited exclusion.

the research questions directly and were excluded. A total of 52 papers were retrieved for evaluation but 38 of these did not meet the inclusion criteria, leaving 15 studies to be critically appraised. Eighteen evidence statements, five clinical practice recommendations (Table 3) and research recommendations were agreed by the Crohn's-DGDG.

Enteral nutrition to induce disease remission

Corticosteroids formed the basis of medical management for active Crohn's disease in adults for many years, although, more recently, other immunomodulatory or biological therapies may be used instead or in combination (Dignass *et al.*, 2010). Corticosteroids are associated with numerous side effects (weight gain, acne, moon face, mood disturbance, insomnia, hyperglycaemia, hypertension) and longer-term health consequences (cognitive impairment, obesity, diabetes, depression, osteoporosis). They are ineffective in maintaining remission, have not been shown to induce mucosal healing (Landi *et al.*, 1992, Modigliani *et al.*, 1990) and are the biggest risk factors in post-operative complications (Dignass *et al.*, 2010).

Enteral nutrition has a role in primary treatment and adjunctive to medical and surgical therapies for treatment of active disease or for nutritional support (Akobeng & Thomas, 2007; Zachos *et al.*, 2007). By contrast to corticosteroids, enteral nutrition is associated with minimal and temporary side effects. Furthermore, exclusive enteral nutrition has been shown to improve mucosal healing in paediatric Crohn's disease (Beattie *et al.*, 1994; Fell *et al.*, 2000; Borrelli *et al.*, 2006). Palatability and social inconvenience can be limiting; however, their impact can be offset by close support from a dedicated dietetic service (King *et al.*, 1997; Lomer *et al.*, 2013). Enteral nutrition continues to be used for nutritional support in adults and is the foundation of treatment in children to ensure adequate growth and development and avoid side effects from drug therapy (Sandhu *et al.*, 2010). However, its use for treatment of Crohn's disease can often be overlooked in adults because of its association with poor adherence, lack of clinician experience in its administration and, commonly, a lack of funding for a dietetic service. Enteral nutrition can be useful in adults when (i) medical therapy is contraindicated; (ii) patients or physicians choose this treatment option (Mowat *et al.*, 2011); (iii) corticosteroids should be avoided (e.g. young adults); and (iv) patients present with or are at risk of malnutrition. Dietary intervention is of paramount importance in all these instances (Dignass *et al.*, 2010).

Included studies and evidence statements

Eight randomised controlled trials (RCTs) assessing exclusive enteral nutrition as a treatment to induce disease remission met the inclusion criteria and were evaluated as summarised in Table 4. Three RCTs compared enteral nutrition with corticosteroids (Lindor *et al.*, 1992; Gorard *et al.*, 1993; Gassull *et al.*, 2002), whereas the remaining five compared elemental with non-elemental enteral nutrition (Giaffer *et al.*, 1990; Rigaud *et al.*, 1991; Mansfield *et al.*, 1995; Verma *et al.*, 2000; Sakurai *et al.*, 2002). Enteral nutrition was taken orally or, if not tolerated, via nasogastric tube. For all studies, the main outcome measure was disease activity index and no study assessed endoscopic or histological healing.

Table 4 Studies included relating to enteral nutrition

Study	Study design and patients	Interventions and duration	Outcome	SIGN
Gassull *et al.* (2002)	MC DB RCT *n* = 62 Active CD VHAI	PEN1 (SHS, Liverpool, UK; high MUFA) *n* = 20 PEN2 (high PUFA) *n* = 23 Pred 1 mg kg^{-1} day^{-1} *n* = 19 ≤4 weeks	Remission VHAI <120 ITT PEN1 20% versus Pred 79% (*P* = 0.0005 ITT PEN2 52% versus Pred 79%*	1+
Giaffer *et al.* (1990)	RCT *n* = 30 CDAI > 150	Elemental (Vivonex; Norwich Eaton, Newcastle upon Tyne, UK) *n* = 16 Polymeric (Fortison; Cow and Gate, Trowbridge, UK) *n* = 14 10 days	Remission CDAI < 150 ITT Elemental 12 (75%) versus Polymeric 5 (36%) = 0.03	1−
Gorard *et al.* (1993)	MC RCT *n* = 42 Active CD DAI	Elemental (Vivonex) *n* = 22 Pred 0.75 mg kg^{-1} day^{-1} 2 weeks, then reducing dose *n* = 20 4 weeks	Remission reduction in DAI ITT Elemental 45% versus Pred 85%*	1−
Lindor *et al.* (1992)	RCT *n* = 19 CDAI > 150	Polymeric (Vital HN; Abbott, Abbott Park, IL, USA) *n* = 9 Pred 0.75 mg kg^{-1} day^{-1} 4 weeks *n* = 10 4 weeks	Remission CDAI reduction by at least 100 ITT Polymeric 33% versus Pred 70%*	1−
Mansfield *et al.* (1995)	RCT *n* = 44 CDAI > 150	Elemental (E028; SHS, Liverpool, UK) *n* = 22 Oligo-peptide (Pepti 2000; Nutricia, Trowbridge, UK) *n* = 22 4 weeks	Remission CDAI reduction by at least 100 Elemental 8 (36%) versus Oligo-peptide 8 (36%) NS*	1−
Rigaud *et al.* (1991)	MC RCT *n* = 30 CDAI > 150	Elemental (Vivonex) *n* = 15 Polymeric (Nutrison; Nutricia, Trowbridge, UK) *n* = 15 >21 days	Remission CDAI < 150 ITT at 28 days Elemental 10 (66%) versus Polymeric 9 (60%) NS*	1−
Sakurai *et al.* (2002)	RCT *n* = 36 CDAI > 150	Elemental (Elental; Ajinomoto, Tokyo, Japan) *n* = 18 Oligo-peptide (Twinline; Otsuka Pharmaceutical, Tokyo, Japan) *n* = 18 6 weeks	Remission CDAI reduction by at least 100 Elemental 67% versus Oligo-peptide 72% NS*	1−
Verma *et al.* (2000)	RCT *n* = 21 CDAI > 150	Elemental (E028) *n* = 10 Polymeric (PD, SHS, Liverpool, UK) *n* = 11 4 weeks	Remission CDAI < 150 OR CDAI reduction by at least 100 Elemental 8 (80%) versus Polymeric 6 (55%) *P* = 0.1	1−

MC, multicentre; DB double-blind; RCT, randomised controlled trial; VHAI, Van Hees activity index; DAI, Dutch activity index; CDAI, Crohn's disease activity index; PEN, polymeric enteral nutrition; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; Pred, prednisolone; ITT, intention-to-treat; NS, nonsignificant.
**P* value not stated.

All studies were critically appraised and resulted in the following evidence statements:

- There is limited weak evidence to indicate that corticosteroids are superior to enteral nutrition administered orally or via a nasogastric feeding tube for inducing clinical remission (Lindor *et al.*, 1992; Gorard *et al.*, 1993; Gassull *et al.*, 2002) SIGN 1−
- There is limited weak evidence to indicate that adherence with enteral nutrition improves effectiveness for induction of clinical remission (Lindor *et al.*, 1992; Gorard *et al.*, 1993; Gassull *et al.*, 2002) SIGN 1−
- There is moderate weak evidence that clinical remission using enteral nutrition taken orally or via a nasogastric tube can be achieved between 10 days and 6 weeks (Giaffer *et al.*, 1990; Rigaud *et al.*, 1991; Lindor *et al.*, 1992; Gorard *et al.*, 1993; Mansfield *et al.*, 1995; Verma *et al.*, 2000; Gassull *et al.*, 2002; Sakurai *et al.*, 2002) SIGN 1−
- There is moderate weak evidence to indicate that non-elemental diets (peptide or polymeric formulas) are as effective as elemental diets taken orally or via a nasogastric tube for inducing clinical remission between 10 days and 6 weeks (Giaffer *et al.*, 1990; Rigaud *et al.*, 1991; Mansfield *et al.*, 1995; Verma *et al.*, 2000; Sakurai *et al.*, 2002) SIGN 1−
- There is limited weak evidence to indicate that an elemental diet is more effective than a polymeric diet for

inducing clinical remission when taken via a nasogastric tube for 10 days (Giaffer *et al.*, 1990) SIGN 1−

Practical considerations

Enteral nutrition may be considered for (i) primary treatment as a sole source of nutrition when other medical therapies are contraindicated (e.g. side effects, drug resistance); (ii) adjunctive treatment with corticosteroids or other medical therapies (e.g. immunosuppressive agents, biological therapy); and (iii) nutritional support when used in conjunction with medical therapy (e.g. in patients with or at risk of malnutrition and/or to improve or maintain nutritional status before surgery and when patients have intercurrent sepsis).

To provide patient choice, counsel patients on the risks and benefits of all available treatment options including enteral nutrition and what formulations are available and how it can be delivered (orally or via enteral tube).

Exclusive enteral nutrition is not indicated in all cases and patient suitability needs to be considered with the patient, family and local IBD team, with appropriate encouragement from all involved to promote compliance. Planned treatment duration should be discussed. A minimum of 10 days is required to induce clinical remission, although considerably longer will be required to achieve mucosal healing (e.g. in paediatrics, it may take 8 weeks to achieve mucosal healing with exclusive enteral nutrition) (Fell *et al.*, 2000).

To determine the clinical response, assess disease activity before starting and during exclusive enteral nutrition.

Osmotic side effects associated with commencing enteral nutrition may be avoided by introducing the enteral formula slowly over several days to reach the target volume.

When using enteral nutrition as a sole source of nutrition, exclude all other foods or drink except still water when the patient is still taking exclusive enteral nutrition. However, in exceptional circumstances to aid adherence, weak black tea or weak black coffee may be allowed.

Food re-introduction diets after exclusive enteral nutrition

After a period of exclusive enteral nutrition, patients are often anxious about which foods to eat and may self-exclude foods fearing that they may exacerbate symptoms and trigger a relapse. Food re-introduction diets are structured dietary protocols (based on exclusion diets) designed to slowly add foods back into the diet after a period of exclusive enteral nutrition. They are often used to identify foods that may induce symptoms and dietary exclusion of such foods may help to maintain remission. However, research is limited and there is debate over whether food re-introduction diets contribute to remission maintenance and which type of diet may be more effective. Their role in maintenance of remission is not recognised in national guidelines for Crohn's disease (Mowat *et al.*, 2011).

Included studies and evidence statements

Three studies met the inclusion criteria (Jones *et al.*, 1985; Riordan *et al.*, 1993; Woolner *et al.*, 1998) and details of these are provided in Table 5. Two studies were RCTs comparing an unrefined carbohydrate rich diet with an elimination diet (Jones *et al.*, 1985) and an exclusion diet with placebo tablets to 'general dietary advice' alongside corticosteroids (Riordan *et al.*, 1993). In Woolner *et al.* (1998), patients were given a choice of either a low-fat, fibre limited, exclusion (LOFFLEX) diet or an elimination diet.

- There is limited moderate evidence that an elimination diet is more effective than 'general dietary advice' and corticosteroids for maintaining remission at 2 years after remission induced by enteral nutrition (Riordan *et al.*, 1993) SIGN 1+
- There is limited weak evidence that an unrefined carbohydrate, fibre rich diet is not effective for maintaining remission (Jones *et al.*, 1985) SIGN 1−
- There is limited weak evidence that an elimination diet is more effective than an unrefined carbohydrate, fibre rich diet for maintaining remission at 6 months (Jones *et al.*, 1985) SIGN 1−
- There is limited weak evidence that a LOFFLEX diet is of similar efficacy to an elimination diet for maintaining remission induced by enteral nutrition at 2 years (Woolner *et al.*, 1998) SIGN 2−
- There is limited weak evidence that patients prefer to follow a LOFFLEX diet and greater compliance is achieved with a LOFFLEX diet compared to an elimination diet (Woolner *et al.*, 1998) SIGN 2−

Practical considerations

After a period of exclusive enteral nutrition, offer patients a food re-introduction diet and, for patients who choose not to follow a food re-introduction diet, support them in returning to their usual diet. Offer all patients regular review to facilitate adherence and ensure nutritional adequacy. Nutritional supplementation (oral nutritional supplements or vitamin/mineral supplements) may be required to address nutritional deficiencies.

It may not be helpful to initiate a food re-introduction diet that requires 'testing' foods for a symptomatic reaction if the diet is started when a patient is weaning off primary medical treatment (e.g. corticosteroids) or starting a new medication for maintenance therapy. Start the testing period once a patient has either stopped the medication or is established on a stable dose. This may not always be

Table 5 Studies included relating to food re-introduction diets

Study	Study design and patients	Interventions and duration	Outcome	SIGN
Jones *et al.* (1985)	RCT $n = 20$ CDAI < 150	Unrefined carbohydrate, fibre rich diet $n = 10$ Elimination diet $n = 10$ 6 months	Relapse CDAI > 150 ITT Unrefined carbohydrate, fibre rich diet $n = 10$ (100%) versus $n = 3$ (30%) $P < 0.05$	1–
Riordan *et al.* (1993)	MC RCT $n = 78$ CD in remission HBI ≤3 using elemental diet	Exclusion diet $n = 40$ Pred $n = 38$ 2 years	Time to clinical relapse HBI >6 ITT Exclusion diet 62% versus Pred 79% $P = 0.048$	1+
Woolner *et al.* (1998)	Prospective uncontrolled $n = 76$ CD in remission HBI ≤3	LOFFLEX diet $n = 48$ Elimination diet $n = 28$ 2 years	Remission at 2 years HBI ≤3 ITT LOFFLEX diet 43.5% versus Elimination diet 45.4% NS*	2–

MC, multicentre; RCT, randomised controlled trial; CDAI, Crohn's disease activity index; HBI, Harvey Bradshaw Index; Pred, prednisolone; LOFFLEX, low-fat fibre limited exclusion; ITT, intention-to-treat; NS, nonsignificant.
**P* value not stated.

practical [e.g. azathioprine (an immunosuppressive agent) can take 3–6 months for optimal therapeutic effect].

Decreasing dietary fibre in stricturing disease

Stricturing Crohn's disease occurs when inflammation causes the bowel wall to thicken and is defined as localised, persistent narrowing, whose functional effects may be judged from prestenotic dilatation (Silverberg *et al.*, 2005). Some strictures are inflammatory, whereas others develop from scar tissue and are fibrotic. They can vary in length and the degree of narrowing. Patients with stricturing Crohn's disease are often advised to follow a low-fibre or low-residue diet to help prevent the risk of bowel obstruction and reduce associated symptoms. There are no national guidelines that have examined the evidence for this practice. Furthermore, the distinction between a low-fibre and a low-residue diet is unclear and there are no universally agreed definitions. Consequently, there is wide variation in clinical practice.

Included studies and evidence statements

Only two relevant published papers were found. They did not meet the inclusion criteria for this question; however, as a result of the paucity of evidence for this question, they were assessed to develop consensus agreement (Woolner *et al.*, 1998; Meier & Gassull, 2004). Meier & Gassull (2004) declare that there was no data to give evidence based recommendations; however, they report that dietary fibre is contraindicated in stricturing Crohn's disease. The paper states that avoidance of coarse and poorly fermented fibre is mandatory in the presence of strictures and that fermentable fibre may contribute to the production of large quantities of gas proximally to a stricture, which in turn could induce uncomfortable symptoms. Woolner *et al.* (1998) state that a low-fibre diet would be less likely to produce obstructive symptoms in patients with inflammatory strictures. This evidence has limited clinical impact because it is only expert opinion.

- There are no clinical trials to support the use of decreasing dietary fibre or residue to reduce the risk of bowel obstruction or to reduce gastrointestinal symptoms in stricturing Crohn's disease
- Dietary fibre is contraindicated in stricturing Crohn's disease. There are no data to give evidence based recommendations (Woolner *et al.*, 1998; Meier & Gassull, 2004) SIGN 4

Practical considerations

Dietary advice for managing strictures in Crohn's disease excludes any foods that may cause a mechanical obstruction or prestenotic pain as a result of excessive gas production [e.g. fibrous parts of fruits and vegetables (skins, seeds, woody stalks etc.), wholegrains, nuts and seeds, gristle on meat, skin on meat or fish, edible fish bones].

Patients following dietary advice for stricturing Crohn's disease should be assessed and reviewed by a dietitian to ensure the diet is nutritionally complete. Nutritional supplementation with oral nutritional supplements or vitamin/mineral supplements may be required. The degree of dietary modification will depend on the nature and extent of the stricture and should be reviewed in line with the medical and/or surgical management in discussion with the IBD team.

Probiotics and prebiotics to induce or maintain disease remission

There is increasing interest in the use of probiotics and prebiotics for manipulation of the gastrointestinal micro-

Table 6 Studies included relating to probiotics

Study	Study design and patients	Interventions and duration	Outcome	SIGN
Guslandi *et al.* (2000)	RCT *n* = 32 CDAI < 150	Probiotic (*Sacchromyces boulardii* + mesalazine) *n* = 16 Control (mesalazine) *n* = 16 6 months	Clinical relapse CDAI > 150 AND CDAI ↑100 ITT Probiotic *n* = 1 (6%) versus Control *n* = 6 (38%) *P* = 0.04	1−
Marteau *et al.* (2006)	MC DB RCT *n* = 98 Resection within 21 days CDAI <200	Probiotic (*Lactobacillus Johnsonii)* *n* = 48 Placebo (maltodextrin) *n* = 50 6 months	Endoscopic recurrence ITT Probiotic *n* = 21 (49%) versus Placebo *n* = 30 (64%) *P* = 0.61	1++
Prantera *et al.* (2002)	DB RCT *n* = 45 Resection and CDAI < 150	Probiotic (*Lactobacillus caseii subspecies rhamnosus)* *n* = 23 Placebo (maltodextrin) *n* = 22 52 weeks	Endoscopic recurrence in patients remaining in clinical remission (Rutgeerts endoscopic score >3) Probiotic: 9/15 (60%) versus Placebo 6/17 (35.3%) *P* = 0.297	1+
Van Gossum *et al.* (2007)	MC DB RCT *n* = 70 Within 7 days of curative ileo-caecal resection	Probiotic (*Lactobacillus Johnsonii)* *n* = 34 Placebo (maltodextrin) *n* = 36 12 weeks	Endoscopic score ITT Probiotic 1.50 versus Placebo 1.22 *P* = 0.48	1+

MC, multicentre; DB, double-blind; RCT, randomised controlled trial; CDAI, Crohn's disease activity index; ITT, intention-to-treat.

biota to counterbalance harmful bacteria. The gastrointestinal microbiota is likely to be involved in the development of chronic inflammation in Crohn's disease (Hedin *et al.*, 2007, 2012; Fiocchi, 2008).

The majority of probiotics and prebiotics have not had their health benefits scientifically proven. European legislation aims to help protect the consumer by indicating that health claims such as 'probiotics' and 'prebiotic fibre' refer to a function in the body and need to be authorised (Food Standards Agency, 2008).

Almost 50% of patients with IBD have tried probiotics (Hedin *et al.*, 2010). In clinical practice, probiotics and prebiotics are not routinely recommended for Crohn's disease, although patients frequently ask about their clinical effectiveness and safety in Crohn's disease.

Included studies and evidence statements

Four RCTs comparing a single strain probiotic to placebo met the inclusion criteria and are summarised in Table 6 (Guslandi *et al.*, 2000; Prantera *et al.*, 2002; Marteau *et al.*, 2006; Van Gossum *et al.*, 2007). Three of the studies assessed the use of a probiotic in the prevention of post-surgical relapse (Prantera *et al.*, 2002; Marteau *et al.*, 2006; Van Gossum *et al.*, 2007), whereas one study assessed the use of a probiotic in remission maintenance with no description of remission induction (Guslandi *et al.*, 2000). No studies assessing the use of prebiotics in Crohn's disease were detected.

- There is no evidence to support the use of prebiotics for inducing or maintaining remission in Crohn's disease
- There is no evidence to support the use of probiotics for inducing remission in Crohn's disease
- There is moderate good evidence that probiotics are ineffective at preventing post-surgical recurrence of Crohn's disease (Prantera *et al.*, 2002; Marteau *et al.*, 2006; Van Gossum *et al.*, 2007) SIGN 1+
- There is limited weak evidence that *S.boulardii* probiotic given in conjunction with mesalazine can increase remission time (Guslandi *et al.*, 2000) SIGN 1−

Practical considerations

The use of prebiotics to induce or maintain remission in Crohn's disease is not currently supported and may have associated gastrointestinal side effects (e.g. abdominal pain, abdominal bloating, diarrhoea and flatulence) (Whelan, 2013). If patients ask about taking probiotics and prebiotics, provide information about the available evidence for taking them in Crohn's disease. Patients should be encouraged to discuss this with their IBD team.

Discussion

These guidelines provide evidence statements, recommendations and practical considerations on enteral nutrition, food re-introduction diets, stricturing disease, and probiotics and prebiotics in the dietary management of Crohn's disease in adults and will improve evidence-based practice. Because much of the evidence is poor quality and limited by the lack of suitable papers for inclusion, research recommendations were proposed.

Adequately powered and well designed RCTs with long term follow-up should focus on the clinical and cost effectiveness and/or safety of dietary treatments using objective and validated assessment of disease activity or other relevant outcome measures.

Several clinical trials have compared the effectiveness of exclusive enteral nutrition to corticosteroids (Zachos *et al.*, 2007), although its effectiveness versus newer and significantly more expensive biological therapies has not been researched to date. Polymeric diets are as effective as elemental diets (Zachos *et al.*, 2007); however, the mechanism of action for the use of exclusive enteral nutrition to treat active Crohn's disease is unknown. Proposed mechanisms have included improved nutritional status, 'bowel rest', reduced dietary antigens, a direct immunomodulatory effect via alterations in fat content and reduced gastrointestinal microbial activity (Tsujikawa *et al.*, 2003; Bannerjee *et al.*, 2004; Gassull, 2004; Lomer *et al.*, 2005; Zachos *et al.*, 2007). In paediatrics, partial enteral nutrition has been shown to be inferior to exclusive enteral nutrition (Johnson *et al.*, 2006), although no studies have been conducted in adults. Optimal duration and indications for giving enteral nutrition based on disease location/severity, effectiveness of enteral nutrition for mucosal healing, benefits of using enteral nutrition as nutritional support or as an adjunct to medical therapy and the effect of a different nutrient composition (specifically fat content and type) would be desirable. Adherence to exclusive enteral nutrition should also be considered to minimise bias in studies comparing dietary and medical therapy.

There is little evidence to support mucosal healing being achieved during a course of exclusive enteral nutrition and serial biopsies would be considered unethical. Alternative measurements of colonic inflammation (e.g. faecal calprotectin) as a proxy for mucosal healing (Papi *et al.*, 2013) may have the potential to guide clinical practice and perhaps also the optimal duration of exclusive enteral nutrition.

Consideration should be given to the most effective type of food re-introduction and/or exclusion diet for maintaining remission and for symptom management.

The nutritional adequacy of dietary advice for stricturing Crohn's disease is important, particularly in relation to the nature and extent of strictures.

Whether probiotics and prebiotics may improve functional gastrointestinal symptoms or have a beneficial effect on the functions of the gastrointestinal microbiota should be investigated further. Subsequent to the searches carried out here, two trials on prebiotics (oligofructose/inulin) have shown no benefit on Crohn's disease activity (Benjamin *et al.*, 2011; Joossens *et al.*, 2012). Interestingly, significantly more patients in the prebiotic arm withdrew from both studies.

These guidelines provide some key recommendations relating to enteral nutrition, food re-introduction diets, stricturing disease, and probiotics and prebiotics (Table 3). Further guidelines for the dietary management of Crohn's disease in adults warrant the inclusion of nutritional assessment and supplementation, supplementary enteral nutrition to maintain disease remission, the effects of enteral nutrition and restrictive diets on body composition and nutritional status, dietary management of oral Crohn's disease, and dietary management of functional gastrointestinal symptoms.

In many patients, functional gastrointestinal symptoms (e.g. abdominal pain, bloating, flatulence and diarrhoea) are more problematic than symptoms as a result of inflammation and may be attributed to irritable bowel syndrome (Simren *et al.*, 2002; Camilleri, 2011). A reduction in short chain fermentable oligosaccharides, disaccharides, monosaccharides and polyols is an emerging dietary management strategy for functional bowel symptoms in Crohn's disease. Although evidence for the clinical effectiveness of reducing such carbohydrates in Crohn's disease is limited (Gearry *et al.*, 2009), interest in this area is increasing.

Access to dietetic services for Crohn's disease across the UK is varied (UK IBD Audit Steering Group, 2007, 2009) and <40% of patients admitted with Crohn's disease were seen by a dietitian (UK IBD Audit Steering Group, 2007, 2009). Furthermore, patients report that access to a dietitian is vital (Jones *et al.*, 2009; Prince *et al.*, 2011) and the need for increased dietetic support is supported by the IBD standards group, who recommend a minimum 0.5 whole time equivalent dietitian for gastroenterology per patient population of 250 000 (IBD Standards Working Group, 2009).

In summary, these guidelines, as developed for registered dietitians, offer evidence-based guidance on the dietary management of adults with Crohn's disease. They aim to increase standardisation in clinical practice and improve patient outcomes in relation to dietary management of this chronic disease.

Acknowledgments

The authors thank Ingrid Darnley, Dr Lee Hooper and Dr Laura Stewart for their assistance in the development of these guidelines. The authors also thank Professor Kevin Whelan for advice on publication and guideline formatting. The authors thank past members of the Crohn's-DGDG, Becky Eyles, Sophie Hamilton, Sian Jones and Rebecca Fisher, for their help in the initial stage of the project and all of the consultation reviewers for their comments on the consultation draft of the guidelines.

Conflict of interests, source of funding and authorship

All authors are practicing dietitians who have worked with adults with Crohn's disease. As such, they have experience and a professional interest in these guidelines. All members of the Crohn's-DGDG signed conflicts of interest forms annually during the development of these guidelines. Signed copies from December 2009 are retained by MCEL and can be inspected by any interested party.

The project was part-funded by the General Education Trust of The British Dietetic Association.All authors contributed to the development of the evidence statements, recommendations and practical considerations and agreed the final document. MCEL and JL were integral to the writing of the final publication, and all of the other authors approved the final draft submitted for publication.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Data S1. UK evidence-based practice guidelines for the dietetic management of Crohn's disease in adults. Professional guideline by The British Dietetic Association, Nov 2011.