


ORIGINAL ARTICLE

Exclusive enteral nutrition in children with inflammatory bowel disease: Physician perspectives and practice

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Key words

Crohn's disease, enteral nutrition, gastroenterologist, pediatrics, surveys and questionnaires.

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Abstract

Background and Aim: Exclusive enteral nutrition (EEN) is recognized internationally as the first line of treatment for children with active Crohn's disease (CD). A survey conducted a decade ago demonstrated that 40% of Australian pediatric gastroenterologists did not think EEN to be an appropriate treatment for CD. This study aimed to explore the current attitudes of Australian and New Zealand (NZ) pediatric gastroenterologists toward the use of EEN in children with inflammatory bowel disease (IBD).

Methods: All practicing pediatric gastroenterologists in Australia and NZ were invited via an existing email network to complete an anonymous online questionnaire.

Results: The questionnaire was completed by 37 respondents (54% response rate), 31 from Australia and 6 from NZ. All respondents felt that EEN definitely or probably has a role in inducing remission for children with newly diagnosed CD. Australian gastroenterologists were more likely to use EEN for relapsed CD or IBD-unclassified than NZ doctors ($P < 0.05$). Adherence was reported to be the greatest disadvantage of EEN. Dietitians were believed to play the most crucial role in EEN administration. Variations in EEN protocols included the use of flavorings or fluids during EEN and different patterns of food reintroduction.

Conclusions: These Australia and NZ pediatric gastroenterologists felt that EEN plays an important role in the induction of remission in children with newly diagnosed CD. However, the perceived role of EEN use in other types of IBD varied. EEN protocols varied widely between centers. Attitudes toward the roles of EEN have altered greatly across Australasia over the last decade.

Introduction

The group of conditions known as inflammatory bowel disease (IBD), which include Crohn's disease (CD), ulcerative colitis (UC), and IBD - unclassified (IBD-U), are characterized by chronic relapsing inflammation of the gastrointestinal tract.¹ Current treatment approaches involve various therapies to reduce inflammation (induction of remission) followed by interventions to maintain control of the inflammation and prevent relapse (maintenance treatment).² In children, therapeutic choices must also take growth and development into account.

The standard treatments for inducing remission in children with active CD include exclusive enteral nutrition (EEN), corticosteroids (CS), or biologic agents.² EEN and CS are the main treatments used following diagnosis in Australasia (Australia and New Zealand [NZ]). Both are equally effective in inducing remission for pediatric CD; however, a larger proportion of children achieve mucosal healing with EEN compared to CS treatment,^{3,4} and EEN enables the avoidance of CS-related adverse effects.

EEN involves drinking a nutritionally complete liquid formula as the sole nutritional source, typically over 8 weeks. Although EEN is now recommended in many guidelines as the preferred intervention to induce remission,^{2,5,6} it is not used universally. A previous report showed that EEN is more commonly used by European than North American gastroenterologists.⁷ Other surveys have found that EEN practices and protocols vary between countries.⁷⁻¹¹

An Australian survey conducted almost 10 years ago also found that only 60% of the responding pediatric gastroenterologists thought that EEN was an appropriate treatment for CD.⁸ In view of the various international consensus statements regarding EEN, along with increased interest in this intervention, it was hypothesized that Australasian EEN practice and attitudes would have changed over the last decade. The primary aim of the current study was to explore the attitudes of Australian and NZ pediatric gastroenterologists toward the use of EEN in children with IBD. The study also aimed to ascertain current EEN practices and protocols in this region.

Methods

Participants. Australian and NZ pediatric gastroenterologists were invited via the Australian Society of Paediatric Gastroenterology, Hepatology and Nutrition (AUSPGHAN) bulletin board to complete an anonymous online questionnaire over an 8-week period. Reminder emails were sent at 4 and 7 weeks. The AUSPGHAN bulletin board comprises currently practicing and previous Australasian pediatric gastroenterologists and trainees. A separate correspondence was sent to the head of each Australasian pediatric gastroenterology unit to confirm the number of practicing physicians and trainees within their state or region.

Questionnaire. The questionnaire (Appendix S1, Supporting information) used was modified from that previously utilized by Day *et al.*⁸ and was administrated using an online platform, Qualtrics© version April 2018 (Provo, UT, USA). The questionnaire was categorized into four sections: participant background, role of EEN in IBD, EEN practices, and reasoning for not recommending EEN. Respondents had five options to rate their previous experience in EEN and the use of EEN in their current unit. The five options were defined as follows: ‘never’ as 0% of the time, ‘rarely’ as approximately 10% of the time, ‘sometimes’ as approximately 25% of the time, ‘regularly’ as approximately 50% of the time, and ‘frequently’ as above 75% of the time.

This study was approved by the subcommittee of the University of Otago Human Ethics Committee (Health).

Statistical analysis. Data were exported from Qualtrics© into IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA) for descriptive statistical analysis. Fisher’s exact test was used to calculate variation difference between countries. Results were expressed in median \pm interquartile range (IQR). Odds ratios (OR) with 95% confidence interval (CI) were calculated where appropriate. *P* value less than 0.05 was considered statistically significant.

Results

Background of respondents. Of 69 currently practicing Australasian pediatric gastroenterologists and trainees, 37 (54%) completed the questionnaire. Of the 37 respondents, 31 (84%) were Australians, and 6 (16%) were New Zealanders. Background details of all respondents were collected (Table 1).

Previous and current experience with EEN. The majority (84%, *n* = 31) of respondents reported that EEN was regularly or frequently used during their period of gastroenterology training. Five Australian respondents (14%) reported that EEN was sometimes or rarely used, and one NZ respondent (3%) reported that EEN was never used during their training.

Of 31 Australian respondents, 29 (94%) used EEN regularly or frequently, whilst 2 (6%) used EEN sometimes in their current departments. All NZ respondents currently used EEN frequently.

Role of EEN in inducing remission in children with IBD. All respondents felt that EEN definitely or probably has a role in inducing remission for children with newly

Table 1 Background characteristics of 37 respondents who completed the online survey of attitudes to exclusive enteral nutrition

	<i>n</i> (%)
Gender (<i>n</i> = 36)	
Male	26 (72)
Age (years)	
<30	0
30–40	10 (27)
41–50	14 (38)
51–60	9 (24)
>60	4 (11)
Australia	31 (84)
New South Wales	8 (26)
Queensland	5 (16)
South Australia	6 (19)
Victoria	11 (35)
Western Australia	1 (3)
New Zealand	6 (16)
Auckland	5 (83)
Canterbury	1 (17)
Practice	
Public hospital academic	35 (95)
Private	12 (32)
Trainee (fellow)	4 (11)

diagnosed CD (Fig. 1). Although 86% (32) of 37 respondents felt EEN definitely or probably has a role in the reinduction of remission for relapsed CD, Australian physicians were more likely to use EEN in this setting than their NZ counterparts (OR 14.5 95% CI 3.2–66.3, *P* < 0.05). All clinicians believed that EEN has some role in induction or reinduction of active CD; however, opinions differed on the role of EEN when disease activity was stratified by severity (Table 2). EEN was 5.5-fold more likely to be used in moderate disease activity than in mild disease activity (OR 5.5 95% CI 2.7–11.3, *P* < 0.01).

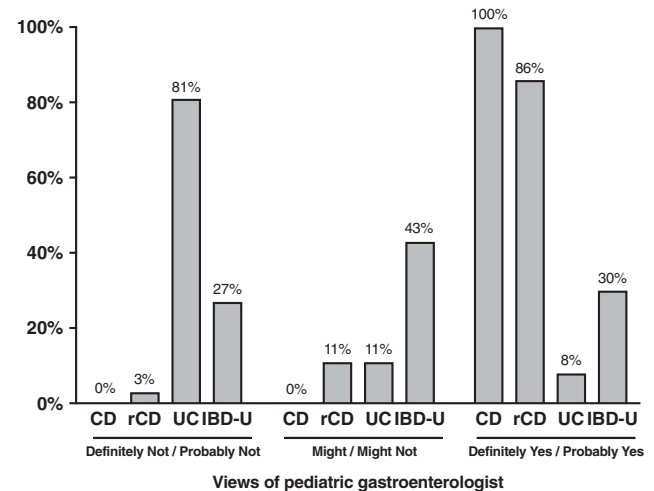


Figure 1 Views of 37 Australian and New Zealand pediatric gastroenterologist on the role of exclusive enteral nutrition in different types of pediatric IBD. CD, Crohn’s disease; UC, ulcerative colitis; IBD-U, inflammatory bowel disease - unclassified.

Table 2 Attitudes of 37 Australasian pediatric gastroenterologists about the role of exclusive enteral nutrition in the induction of remission in newly diagnosed and relapsed Crohn’s disease stratified by disease severity

Disease Severity	Australia and New Zealand (n (%))
Newly diagnosed Crohn’s disease	
Mild disease activity	27 (73)
Moderate disease activity	33 (89) [†]
Severe disease activity	32 (87)
Relapsed Crohn’s disease	
Mild disease activity	23 (62)
Moderate disease activity	33 (89)
Severe disease activity	28 (76)

[†]Odds ratio 5.5 95% confidence interval 2.7–11.3, *P* < 0.01 compared to mild disease activity.

In contrast to the perceived role of EEN in CD, 30 (81%) respondents felt that EEN was definitely not or probably not appropriate in UC. The views of the role of EEN in IBD-U were more variable (Fig. 1). The Australian doctors were 8-fold more likely to use EEN in IBD-U than the NZ doctors (OR 8.3 95% CI 2.9–23.6).

The advantages and disadvantages of EEN. The respondents felt that the main benefits of EEN were avoidance of steroids (95%, 35/37), nutritional improvements (95%, 35/37), and correction of growth failure (84%, 31/37) (Fig. 2). The respondents commented that the biggest disadvantage of EEN was adherence (81%, 30/37), followed by being more time intensive for the families (62%, 23/37). The need for a multidisciplinary team and time requirements for the team were thought to be disadvantages by 49% (*n* = 18) of respondents (Fig. 2).

EEN practices. Of 37, 32 (86%) gastroenterologists reported a median of 11 (IQR 5–17) children diagnosed with CD in 2017; 28 Australian physicians diagnosed a median of 14 (IQR 6–20) patients; and 4 NZ physicians diagnosed a median of 11 (IQR

5–15) patients. Of the newly diagnosed patients, a median of 10 (IQR 5–13) children were treated with EEN: median 9 (IQR 5–12) patients in Australia and 14 (IQR 6–18) patients in NZ.

Most physicians (92%, 34/37) would always or often use EEN in children with ileocolonic disease, 86% (32/37) for upper and lower gut disease, 73% (27/37) for isolated upper gut disease, 72% (26/36) for isolated colonic disease, and 25% (9/26) for perianal disease. Only one respondent reported using EEN for orofacial CD.

Clinicians believed the following factors influenced the success of EEN in children: involvement of parent(s) (100%), dietitian support and child’s personality (97%, 36/37), nursing support (95%, 35/37), child’s age (76%, 28/37), disease location (68%, 25/37), type of formula (65%, 24/37), growth potential (51%, 19/37), financial coverage (46%, 17/37), disease severity (43%, 16/37), and length of symptoms (16%, 6/37).

Most (95%, *n* = 35) of the 37 respondents utilized polymeric formulae for EEN. Three doctors also used an elemental formula, and two used a semielemental formula. Seven separate formula brands were mentioned by respondents. When asked about the reason for choosing the particular formula, taste (78%, 29/37) was mentioned most frequently, followed by availability (68%, 25/37), cost (27%, 10/37), and composition (19%, 7/37). Hospital recommendation and easy portability were also mentioned by 8% (*n* = 3) of respondents.

Half the clinicians (*n* = 18) permitted patients to add flavoring agents to the formula. Two thirds of these practitioners mentioned two flavoring brands, whilst four others would base decisions on their dietitian’s advice. Ten physicians (27%) would allow fluids (such as black tea, soft drinks, diluted fruit juice, barley water, and jelly) in addition to water whilst on EEN. Several of these doctors would also allow boiled lollies and chewing gum.

Most (95%, *n* = 35) of the 37 gastroenterologists prescribed EEN for 6–8 weeks. Two gastroenterologists (5%) typically prescribed EEN for longer periods (8–10 weeks and 10–12 weeks respectively).

When asked who assists in the administration of EEN in their center, respondents commented that a dietitian plays the

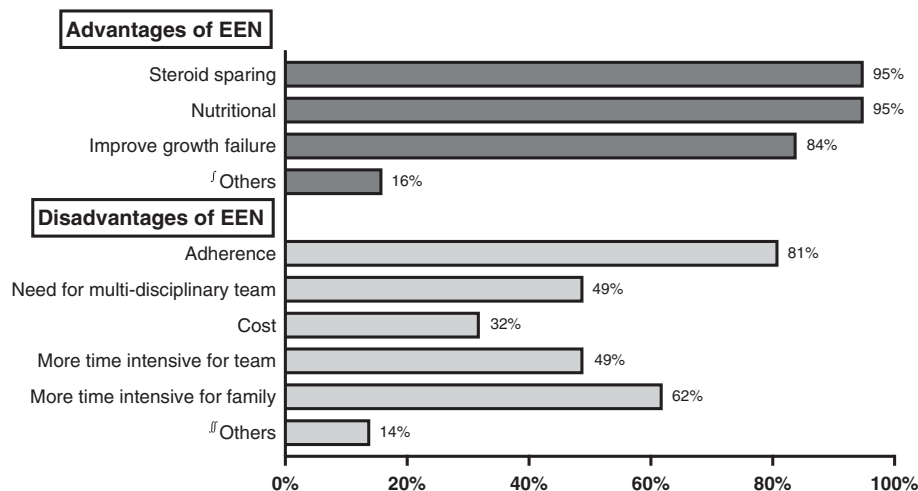


Figure 2 Respondents’ opinions of the advantages and disadvantages of recommending exclusive enteral nutrition (EEN).

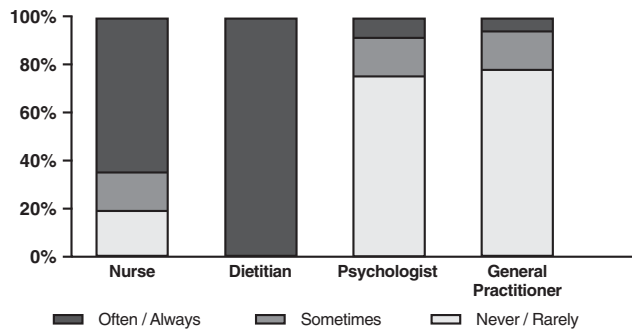


Figure 3 Physicians' views regarding the involvement of other health professionals in the administration of exclusive enteral nutrition. (■), Often/always; (■), sometimes; (□), never/rarely.

most crucial role (Fig. 3). Nurses were seen as playing important roles: 65% (24 of 37) reported that nurses were always or often involved. The patient's general practitioner or a psychologist was involved infrequently. The majority of respondents provided support for the additional costs to facilitate EEN: 84% ($n = 31$) provide formula and pumps, and 81% ($n = 30$) provide equipment (such as tape, tubing, and syringes) when required.

Assessment used to define outcomes of EEN. The main modalities used by the 37 respondents to assess the outcomes of EEN were improvements in clinical status (97%, $n = 36$), nutritional indicators (95%, $n = 35$), blood-based inflammatory markers such as C-reactive protein (97%, $n = 36$), and

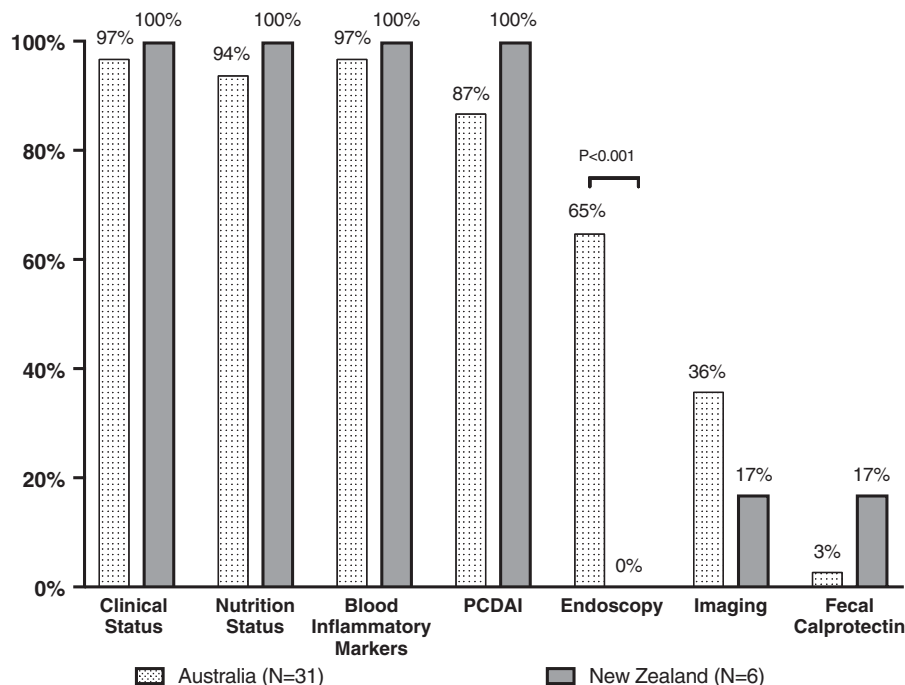


Figure 4 Pediatric gastroenterologists' opinions of assessment methods to define the outcome of exclusive enteral nutrition for induction of remission. Results presented in percentages. (▨), Australia ($n = 31$); (■), New Zealand ($n = 6$). PCDAI, Pediatric Crohn's Disease Activity Index.

the Pediatric Crohn's Disease Activity Index (89%, $n = 33$) (Fig. 3). Endoscopic reassessment was seen as relevant by 54% ($n = 20$) of respondents: this was considered more commonly by Australian clinicians ($P < 0.001$) (Fig. 4). Only two clinicians utilized fecal calprotectin for monitoring EEN outcomes.

Reintroduction of food following EEN. The practice of reintroduction of food following EEN varied between clinicians. Of 34 respondents, 26 (76%) allow one normal food meal at a time; 15 of 33 (45%) would reintroduce food based on fiber content/residue (i.e. minimal residue first, then low residue and higher residue after), while 5 of 30 (17%) would recommend low-allergen foods first.

Other routine medical treatments started during EEN. More than half (54%, $n = 20$) of the 37 gastroenterologists typically prescribed one or more drugs during EEN in newly diagnosed active CD. Concurrent medical treatments were thiopurine (68%, $n = 25$), methotrexate (32%, $n = 12$), 5-aminosalicylic (16%, $n = 6$), and CS (3%, $n = 1$). Medical treatments were either started immediately or within 4 weeks after commencing EEN.

Maintenance enteral nutrition. Following completion of EEN, 19 (51%) physicians would recommend some form of maintenance enteral nutrition (MEN). Of those who gave specific recommendations, six respondents would recommend MEN to provide 30–50% of estimated energy requirements, and another six respondents encouraged drinking between 1 and 5 cartons of formula daily.

Discussion

EEN is recognized and recommended to be the first line of induction treatment for CD in children. This study confirmed that Australia and NZ pediatric gastroenterologists believe that EEN plays an important role in CD, especially in newly diagnosed children. This reflects that the practice in both countries is consistent with international recommendations.^{2,5,6} However, EEN protocols varied widely between centers.

The utilization of EEN for pediatric CD has changed significantly in the past decade. The current study found that all respondents would definitely or probably use EEN to induce remission in newly diagnosed CD compared to a previous survey, which found that only 60% of respondents felt EEN to be appropriate for CD.⁸ The reported rates of usage of EEN for active CD are greater than that reported by European and Japanese physicians.^{7,9,12} In the current study, EEN was more commonly used for CD with moderate to severe disease activity than for children with mild disease activity. Although the survey instrument was not able to elucidate the reasons for this variation, it may reflect that EEN is seen as less appropriate or too difficult (whether by physicians or patients) in the setting of mild disease activity.

Exposure to the use of EEN during earlier gastroenterology training influences current EEN practices.¹⁰ The current study found two clinicians who never or rarely used EEN during their training, compared to nine clinicians in the earlier Australian survey.⁸ It is common to encourage gastroenterology trainees to complete their training in different hospitals or to pursue an international fellowship. The various training sites may have increased trainees' exposure to EEN, which may have influenced the increased use of EEN in both countries.

All treatments, including EEN, used in individuals with IBD have potential advantages and disadvantages. Adherence to EEN is the greatest disadvantage highlighted by previous studies^{8,13,14} and in the current study. One way to ensure adequate intake during EEN is to administer the formula via a nasogastric or a gastrostomy tube. Gastroenterologists from the United Kingdom and Canada were more likely to use nasogastric or gastric tubes over oral feeds to aid adherence.^{10,15} This practice may reflect the type of enteral formula utilized: typically, semielemental or elemental formulae require administration via a tube due to less acceptable taste characteristics.

The European Crohn's and Colitis Organisation (ECCO) and European Society of Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) consensus guidelines have recommended that EEN is administered over 6–8 weeks.² The majority of the Australasian practitioners in the current and the previous survey utilize EEN over 6–8 weeks.⁸ However, other international practices differ widely; previous surveys indicated that 52% of Swedish clinicians recommend 6 weeks' duration, whilst 30% of North American clinicians recommend less than 6 weeks and 46% recommend 6–8 weeks' duration.^{10,12} In contrast, in a different assessment, Japanese gastroenterologists only prescribed EEN for a mean duration of 15.9 days in children with active CD.⁹

Various types of enteral formula can be used for EEN. In Australasia, 95% of physicians use polymeric formulae. A recent global survey (that included Canada, USA, UK, Spain, and other European countries) found that 88% of respondents use polymeric formula.¹³ In contrast, Japanese clinicians almost universally prefer elemental formulae.⁹ The most recent Cochrane study and a

separate randomized control trial found no significant difference between elemental and polymeric formulae in terms of inducing remission for CD.^{14,16} In the current study, taste and availability were highly rated by clinicians to influence the choice of a particular formula for EEN. Although polymeric formulae are less expensive than elemental formulae, only 27% respondents felt this to be the reason for choosing polymeric formula.

The use of flavoring agents or inclusion of other foodstuffs (such as boiled lollies) in EEN protocols varies widely.¹³ Half of the physicians in the current study would allow flavoring, and about a third of physicians allow some clear fluids in addition to water. Whilst the motivation is to avoid taste fatigue and enhance adherence, there is no clear data to support this practice. Furthermore, several reports demonstrate that response rates to partial enteral nutrition are lower than EEN, suggesting that these additional elements may not be beneficial overall.^{17,18} In contrast, limited evidence from studies evaluating the CD exclusion diet and the specific carbohydrate diet indicate that remission can be induced with diets containing selected whole foods.^{19,20} Further work is still required to ascertain optimal protocols for EEN in children.

Another variation in EEN protocols is the way solid foods are recommenced at the end of the course of EEN. Although there is no clear data to support any practice, the ECCO and ESPGHAN consensus panel suggested progressive reduction of formula volume every 2–3 days over a 2–3-week period whilst steadily increasing solid foods.² In the current study, three-quarters of the respondents reporting reintroducing one normal food meal at a time whilst reducing formula volumes progressively. Recently, Faiman *et al.*²¹ reported that rapid food introduction over 3 days is safe and equally effective to reintroduction of food over 5 weeks. Retrospective studies show that food intolerances are uncommon following reintroduction of normal food, suggesting that a low-allergen approach is unnecessary and may unnecessarily prolong the period of nutritional change.^{22,23}

Routine commencement of a maintenance drug during EEN is a common practice.¹⁰ Half of the gastroenterologists in the current study typically commence a medical therapy (most commonly a thiopurine) during EEN. Given the delay in onset of response to these drugs, they are unlikely to enhance the benefits of EEN. However, side effects (such as nausea) secondary to an immunomodulator could adversely impact the outcomes of EEN. Although the early introduction of an immunomodulator was found to sustain remission after induction with CS in moderate to severe CD,²⁴ this has not been demonstrated when EEN is used to induce remission. Only one respondent in the current study reported the regular use of another agent that also induces remission (CS) during EEN: there is no current evidence regarding this practice.

The majority of respondents in the current study used clinical, nutritional, and biochemical parameters to define the success of EEN. Two-thirds of the Australian doctors also reported endoscopic improvement to be an additional factor in defining EEN success: none of the NZ respondents reported this. Although the survey was unable to elucidate the reasons for this variation in approach, this may be explained by a recent Australian report showing that children with complete mucosal healing on early endoscopic re-evaluation following EEN were found to have prolonged remission up to 3 years.²⁵

The information provided by this group of pediatric gastroenterologists illustrates key similarities and variations of EEN practice across the region. The design of the study did not enable

clarification of several aspects such as EEN outcomes and did not capture the attitudes of other disciplines involved in the administration of EEN. The completed response rate was 54% of consultants and trainees across the two countries; however, the geographical spread of the respondents suggests that the findings are likely representative of the region. The use of an online survey document following an email invitation may lead to a selection bias. This methodology also prevents the cross-validation of responses by objective measures and may have introduced recall bias in the reporting number of patients commenced on EEN. The total number of paediatric gastroenterologists and trainees in Australia is substantially larger than in NZ, meaning that the findings of the study may be biased toward Australia and may give wide CIs in the NZ findings.

In conclusion, the current study found a shift in the attitudes of Australasian paediatric gastroenterologists toward the use of EEN in children with newly diagnosed CD over the last decade. However, there remain variations in the attitudes toward EEN in other IBD types, and variations of practice were observed between the respondents. Consideration should be made regarding ways to further enhance consistency, including focused assessments of aspects of EEN protocols: findings arising should enhance patient outcomes.

REFERENCES

- Levine A, Koletzko S, Turner D *et al*. ESPGHAN revised porto criteria for the diagnosis of inflammatory bowel disease in children and adolescents. *J. Pediatr. Gastroenterol. Nutr.* 2014; **58**: 795–806.
- Ruemmele FM, Veres G, Kolho KL *et al*. Consensus guidelines of ECCO/ESPGHAN on the medical management of paediatric Crohn's disease. *J. Crohns Colitis.* 2014; **8**: 1179–207.
- Swaminath A, Feathers A, Ananthakrishnan AN, Falzon L, Li Ferry S. Systematic review with meta-analysis: enteral nutrition therapy for the induction of remission in paediatric Crohn's disease. *Aliment. Pharmacol. Ther.* 2017; **46**: 645–56.
- Berni Canani R, Terrin G, Borrelli O *et al*. Short- and long-term therapeutic efficacy of nutritional therapy and corticosteroids in paediatric Crohn's disease. *Dig. Liver Dis.* 2006; **38**: 381–7.
- Critch J, Day AS, Otley A, King-Moore C, Teitelbaum JE, Shashidhar H. Use of enteral nutrition for the control of intestinal inflammation in pediatric Crohn disease. *J. Pediatr. Gastroenterol. Nutr.* 2012; **54**: 298–305.
- Forbes A, Escher J, Hebuterne X *et al*. ESPEN guideline: clinical nutrition in inflammatory bowel disease. *Clin. Nutr.* 2017; **36**: 321–47.
- Levine A, Milo T, Buller H, Markowitz J. Consensus and controversy in the management of pediatric Crohn disease: an international survey. *J. Pediatr. Gastroenterol. Nutr.* 2003; **36**: 464–9.
- Day AS, Stephenson T, Stewart M, Otley AR. Exclusive enteral nutrition for children with Crohn's disease: use in Australia and attitudes of Australian paediatric gastroenterologists. *J. Paediatr. Child Health.* 2009; **45**: 337–41.
- Ishige T, Tomomasa T, Tajiri H, Yoden A; Japanese Study Group for Pediatric Crohn's Disease. Japanese Study Group for Pediatric Crohn's D. Japanese physicians' attitudes towards enteral nutrition treatment for paediatric patients with Crohn's disease: a questionnaire survey. *Intest. Res.* 2017; **15**: 345–51.
- Stewart M, Day AS, Otley A. Physician attitudes and practices of enteral nutrition as primary treatment of paediatric Crohn disease in North America. *J. Pediatr. Gastroenterol. Nutr.* 2011; **52**: 38–42.
- Whitten KE, Rogers P, Ooi CY, Day AS. International survey of enteral nutrition protocols used in children with Crohn's disease. *J. Dig. Dis.* 2012; **13**: 107–12.
- Grafors JM, Casswall TH. Exclusive enteral nutrition in the treatment of children with Crohn's disease in Sweden: a questionnaire survey. *Acta Paediatr.* 2011; **100**: 1018–22.
- Lawley M, Wu JW, Navas-Lopez VM *et al*. Global variation in use of enteral nutrition for pediatric Crohn disease. *J. Pediatr. Gastroenterol. Nutr.* 2018; **67**: e22–9.
- Narula N, Dhillon A, Zhang D, Sherlock ME, Tondeur M, Zachos M. Enteral nutritional therapy for induction of remission in Crohn's disease. *Cochrane Database Syst. Rev.* 2018; **4**: CD000542.
- Terry A, Grogan JL, Casson DH, Dalzell AM, El-Matary W. Tube feeding therapy in paediatric Crohn's disease. *Aliment. Pharmacol. Ther.* 2011; **34**: 260–1.
- Grogan JL, Casson DH, Terry A, Burdge GC, El-Matary W, Dalzell AM. Enteral feeding therapy for newly diagnosed pediatric Crohn's disease: a double-blind randomized controlled trial with two years follow-up. *Inflamm. Bowel Dis.* 2012; **18**: 246–53.
- Johnson T, Macdonald S, Hill SM, Thomas A, Murphy MS. Treatment of active Crohn's disease in children using partial enteral nutrition with liquid formula: a randomised controlled trial. *Gut.* 2006; **55**: 356–61.
- Lee D, Baldassano RN, Otley AR *et al*. Comparative effectiveness of nutritional and biological therapy in North American children with active Crohn's disease. *Inflamm. Bowel Dis.* 2015; **21**: 1786–93.
- Sigall-Boneh R, Pfeffer-Gik T, Segal I, Zangen T, Boaz M, Levine A. Partial enteral nutrition with a Crohn's disease exclusion diet is effective for induction of remission in children and young adults with Crohn's disease. *Inflamm. Bowel Dis.* 2014; **20**: 1353–60.
- Suskind DL, Cohen SA, Brittnacher MJ *et al*. Clinical and Fecal Microbial Changes With Diet Therapy in Active Inflammatory Bowel Disease. *J. Clin. Gastroenterol.* 2018; **52**: 155–63.
- Faiman A, Mutalib M, Moylan A *et al*. Standard versus rapid food reintroduction after exclusive enteral nutritional therapy in paediatric Crohn's disease. *Eur. J. Gastroenterol. Hepatol.* 2014; **26**: 276–81.
- Day AS, Whitten KE, Lemberg DA *et al*. Exclusive enteral feeding as primary therapy for Crohn's disease in Australian children and adolescents: a feasible and effective approach. *J. Gastroenterol. Hepatol.* 2006; **21**: 1609–14.
- Shergill-Bonner RBM, Torrente F, Heuschkel R. Food re-introduction after exclusion enteral nutrition - a clinical experience. *J. Pediatr. Gastroenterol. Nutr.* 2007; **44**: E36.
- Punati J, Markowitz J, Lerer T *et al*. Effect of early immunomodulator use in moderate to severe pediatric Crohn disease. *Inflamm. Bowel Dis.* 2008; **14**: 949–54.
- Grover Z, Burgess C, Muir R, Reilly C, Lewindon PJ. Early mucosal healing with exclusive enteral nutrition is associated with improved outcomes in newly diagnosed children with luminal Crohn's disease. *J. Crohns Colitis.* 2016; **10**: 1159–64.

Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:

Appendix S1. Questionnaire for the study: 'exclusive enteral nutrition in children with inflammatory bowel disease: physician perspectives and practice' (adopted from online survey questions).