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ORIGINAL ARTICLE

Patterns of vitamin D testing and supplementation for children with inflammatory bowel disease in Australasia

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Abstract

Background and Aim: For children with inflammatory bowel disease (IBD), optimal levels of vitamin D are ascribed anti-inflammatory and essential immune system roles that are associated with reduced disease activity, lower postoperative recurrence, and higher quality of life. International guidelines for vitamin D testing and supplementation provide inconsistent recommendations. The aim of this study was to survey Australasian pediatric gastroenterologists to ascertain current practices of vitamin D testing and supplementation for children with IBD.
Methods: Members of the Australian Society of Pediatric Gastroenterology, Hepatology and Nutrition were invited to complete an online survey. Respondents were asked to provide information on frequency of vitamin D testing and supplementation, adherence, and benefits of vitamin D to children with IBD.
Results: Thirty-two (54%) pediatric gastroenterologists completed the survey: 27 (84%) from Australia and 5 (16%) from New Zealand. The majority (90%) tested vitamin D levels at diagnosis and follow up, although testing frequency varied (1–3 times/year) and only 8 (28%) tested seasonally. While 28 (88%) recommended supplementation based on serum levels, inconsistent cutoff values were used. Most respondents ($n = 27$) recommended Stoss (single dose) or vitamin D3 (daily for 8–12 weeks). The majority (84%) rated the overall benefit of optimal vitamin D levels at ≥6/10, although fewer (54%) rated the benefit to disease activity at ≥6/10.
Conclusions: The results indicate that standardized guidelines for vitamin D testing and supplementation for clinicians caring for children with IBD throughout Australasia are required. Consensus statements may optimize the care of children with IBD in this diverse geographical region.

Introduction

Vitamin D has numerous important roles for children with inflammatory bowel disease (IBD). Optimal levels are ascribed anti-inflammatory and essential immune system roles,[1–3] and have been linked to such benefits as reduced disease activity, less frequent relapses, lower postoperative recurrence, higher quality of life, and improved response to particular IBD treatments.[4,5] Suboptimal levels of vitamin D, known as hypovitaminosis D, may be caused by reduced skin exposure to sunlight, decreased oral intake, nutrient malabsorption, and gastrointestinal losses.[2,6]

Screening for hypovitaminosis D should be carried out on all children with IBD, regardless of their clinical subtype.[7] While concentrations are typically lower at the time of diagnosis, many children remain deficient following treatment and during follow up, and should be monitored accordingly.[7] Screening is endorsed at diagnosis and then at least yearly, with particular attention to seasonality, as well as during active and asymptomatic periods.[8] The optimal serum level of vitamin D varies throughout the literature, but it is now generally considered that a level of ≥75 nmol/L (≥30 ng/mL) may be required for those with IBD in order to optimize the ascribed benefits.[4,9] Correction of hypovitaminosis D requires supplementation in order to increase vitamin D levels sufficiently. Ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3) are the most frequently used forms of oral supplement, with evidence supporting the preferential use of cholecalciferol due to superior efficacy.[6,10,11] A number of regimens for supplementation of vitamin D2/D3 may be used, such as daily, weekly, or one-off high dose vitamin D3 (Stoss therapy).[12]

For clinicians working with children with IBD, access to evidence-based guidance on vitamin D testing and supplementation is important in order to optimize care for their patients. National and international scientific societies focused on pediatric gastroenterology, hepatology, and nutrition bring together expertise to develop evidence-based clinical practice guidelines.

Several organizations have published recommendations for the testing and supplementation of vitamin D for children with IBD; however, no standardized approach is presented across these.[13–15] In New Zealand (NZ), there is a national clinical guideline available for the management of children with IBD that states to test vitamin D at diagnosis, and annually thereafter, although does not include guidance on optimal levels to be attained or supplementation.[16] No comprehensive guideline has been developed specifically for use across Australasia.

The objective of this study was to distribute an online survey to pediatric gastroenterologists throughout Australasia in order to review patterns of vitamin D testing and supplementation for children with IBD. The aim was to establish whether patterns emerge in testing or supplementation frequency that may be used to guide the development of a comprehensive Australasian guideline in order to standardize care and, therefore, maximize benefit to the patient.

Methods

Ethics. All participants provided consent to take part in the study, which was reviewed and approved by the University of Otago Human Ethics Committee, NZ (D22/40).

Study design and participants. This study was a descriptive survey of practice and attitudes carried out among pediatric gastroenterologists throughout Australasia. Respondents were invited to participate via the Australian Society of Pediatric Gastroenterology, Hepatology and Nutrition (AuSPGHAN) email list. The study invitation and link to study documentation was distributed by email to AuSPGHAN members by the PEDiatric Australasian Gastroenterology Research NEtwork (PEDAGREE). Reminders were sent after 2 weeks to maximize response rates.

Study outcomes. Data were collected via electronic survey (Cognito forms, Columbia, South Carolina, US). In addition to general, background data, key variables focused on clinical experience and caseload, vitamin D testing and supplementation, adherence, and opinion on benefits of vitamin D to children with IBD. Questions regarding perceived adherence and perceived benefit were referenced to a 1–10 scale (10 being most adherent or most beneficial). The survey content was reviewed and approved by the Executive members of PEDAGREE.

Statistical analysis. Descriptive analysis was predominantly performed. Numbers and percentages provided to indicate between group differences. Ordinal variables are further explored where possible using the chi-squared (χ^2) goodness-of-fit test with Phi effect size, with Phi results closer to 1.0 indicating a stronger effect size. Results considered significant at a level $P \leq 0.05$. Analysis carried out using SPSS version 28.0.1, IBM Corp, Armonk, NY, US.

Results

Participants. Fifty-nine AuSPGHAN members were invited to participate, with 32 (54%) completing the survey (Table 1). Twenty-seven (84%) were based in Australia and five (16%) from NZ. The respondents reported having a mean duration of caring for children with IBD of 15.5 years (SD 8.7, range 4–37). Most respondents (78%) had an individual caseload of less than 100 children with IBD and a shared caseload in their center of more than 200 children (75%).

Table 1 Region of practice and clinical encounter information for participating Australasian clinicians.

Variable	Category	*N* (%)
New Zealand region	North Island	4 (13)
	South Island	1 (3)
Australia region	Queensland	3 (10)
	New South Wales	10 (31)
	Victoria	10 (31)
	South Australia	2 (6)
	Western Australia	2 (6)
Attends satellite/outreach clinics	Yes	13 (41)
Frequency of IBD focused out-patient clinics per month	<5	17 (53)
	6–10	9 (28)
	>10	4 (13)
	Other†	2 (6)
Frequency of evaluation of children with IBD as in-patients	Daily	4 (13)
	At least 1/week	12 (37)
	Less 1/week	12 (37)
	Varies	4 (13)
Work as part of a multi-disciplinary team caring for children with IBD	Yes	24 (75)
	No	6 (19)
	Other‡	2 (6)

†Frequency of clinics was variable.
‡Multidisciplinary clinic was not available at all sites respondents worked in.

Vitamin D testing. The majority of respondents tested vitamin D levels at diagnosis and during routine follow up (Fig. 1). A small number (2–3 participants) carried out testing at these time points only if a patient had one or more specific risk factor for hypovitaminosis D: stated reasons were darker skin type, severe disease, or poor nutritional status. The frequency of testing was relatively evenly distributed between once, twice, or three times per year, with eight (28%) changing their testing frequency depending on the season. NZ clinicians were more likely to carry out seasonal testing than those in Australia (χ^2 5.2 [Phi 0.42], $P = 0.05$). Of the 29 respondents who routinely test vitamin D levels (three did not routinely test), six (21%) utilized local, national, or international guidelines to inform their testing schedule. NZ clinicians were more likely to use these resources than their Australian counterparts ($N = 4/4$ (100%) *versus* 2/25 (8%); χ^2 17.8 (Phi 0.78), $P < 0.001$). The guidelines utilized were stated as being national NZ guidelines,[16] local guidelines, or British Society of Pediatric Gastroenterology, Hepatology, and Nutrition (BSPGHAN) guidelines.[15]

Vitamin D supplementation. Most respondents supplemented children with IBD according to the results of serum levels (Fig. 2). Two stated that they recommended supplementation in children with poor nutrition. One (4%) supplemented at

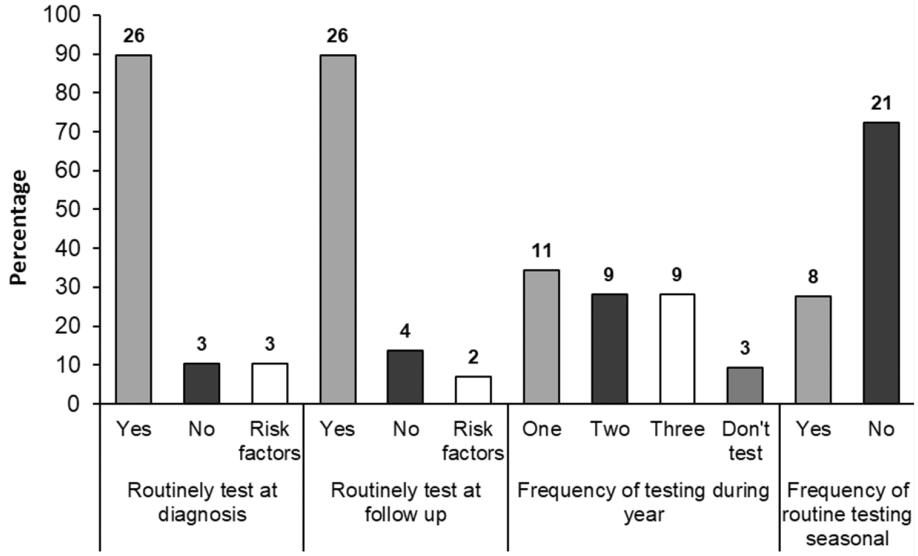

Figure 1 Frequency of answers to variables relating to vitamin D testing among AuSPGHAN respondents. Numbers at the top of bars represent actual response number, number answering each variable dependent on answer to previous question.

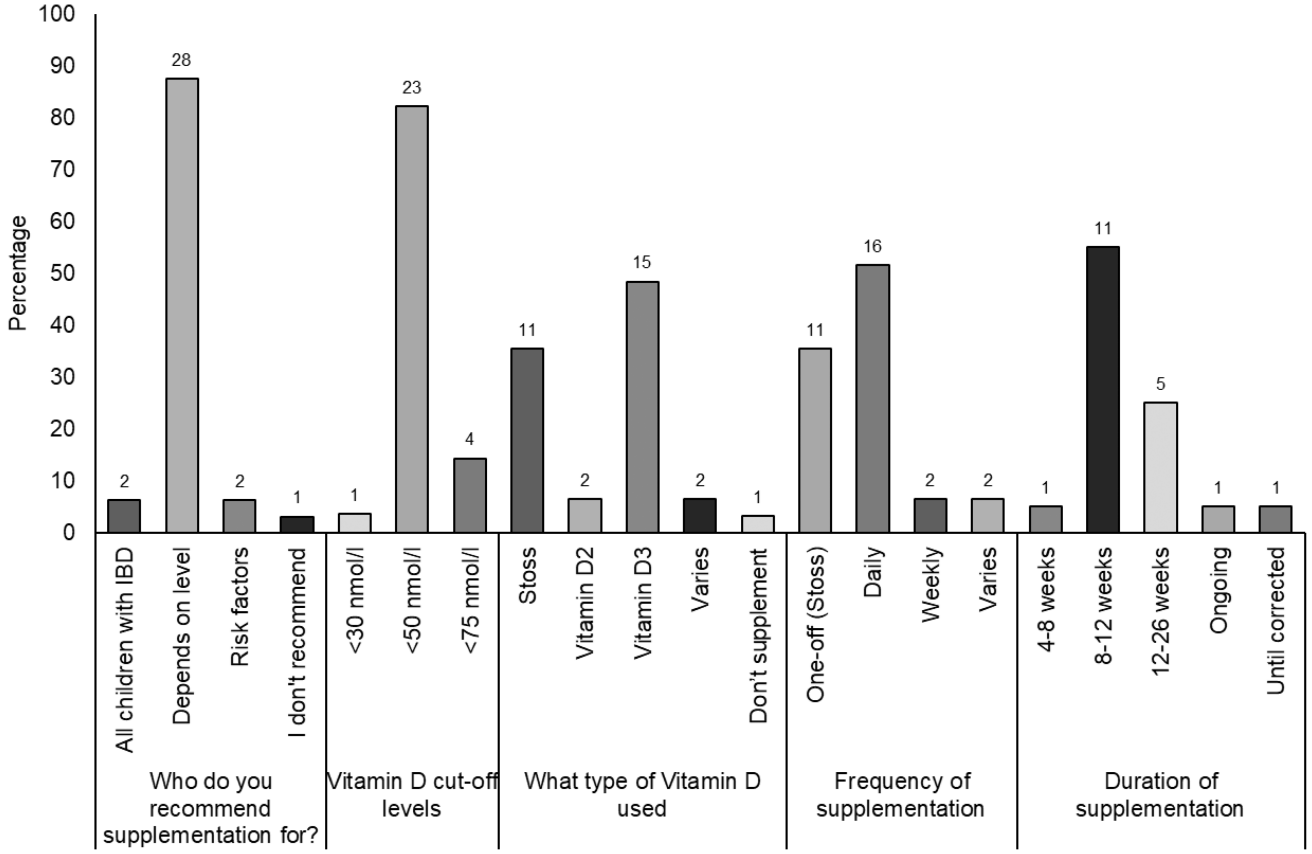

Figure 2 Frequency of answers to variables relating to vitamin D supplementation among Australasian pediatric gastroenterology respondents. Numbers at the top of bars represent actual response number, number answering each variable dependent on answer to previous question.

levels <30 nmol/L, 23 (82%) at levels <50 nmol/L, and 4 (14%) at levels <75 nmol/L. Most respondents ($N = 27$) recommended Stoss (as a single dose) or vitamin D3 (given daily for 8–12 weeks).

Retesting of vitamin D levels following supplementation was carried out by 24 (80%) of the clinicians (of those that use supplementation): most ($N = 13$) retesting 3 months after supplementation. Four would retest after less than 3 months and seven after 6 months. Twelve (38%) clinicians utilized local, national, or international guidelines to inform their supplementation schedule, with four different guidelines stated, from: New Zealand ($N = 2$),[16] European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) ($N = 1$), Royal Children's Hospital Melbourne (RCH)[17] ($N = 6$), and local ones ($N = 4$). The use of guidelines was not associated with the use of a particular cutoff level of vitamin D (χ^2 1.2 [Phi 0.0.2], $P = 0.56$), or the type of supplementation used when limited to those stating Stoss, vitamin D2 or D3 (χ^2 1.5 [Phi 0.23], $P = 0.46$).

The clinicians reported that a variety of factors influenced their decision to use a particular type of supplementation (Fig. 3). These highlight that factors related to the patients, such as adherence, tablet burden, efficacy, and ease of administration, influenced the use of Stoss. Factors relating to ease of availability and being "standard practice" influenced the use of vitamin D3. Almost all of the respondents reported that they rarely ($N = 21$) or never ($N = 10$) encountered side effects due to vitamin D supplementation. One respondent reporting sometimes seeing side effects (not specified).

Adherence. Half of the respondents reported their patients had above-average (6–10 on adherence scale) adherence, while the other half reported adherence of <5. The reported median rating was numerically higher (7/10) for children receiving Stoss rating than those receiving vitamin D2 (6/10) or vitamin D3 (5/10).

Benefit of optimal vitamin D levels. The majority (84%) of respondents rated the overall benefit of optimal vitamin D levels for children with IBD to be ≥6/10. Fewer (56%) of the clinicians felt that optimal vitamin D levels benefited disease activity at a rating ≥6/10 (Fig. 4). Free-text responses relating to the benefit of optimal vitamin D included improved bone health ($N = 2$), enhanced mood ($N = 1$), and reduced IBD flares ($N = 1$).

Discussion

Patterns of vitamin D testing and supplementation for children with IBD have been shown in this study to be variable throughout Australasia. Despite a subgroup of clinicians using local, national, or international guidelines to inform their practice, this factor did not appear to standardize their approach to testing or supplementation. The opinion of adherence to vitamin D

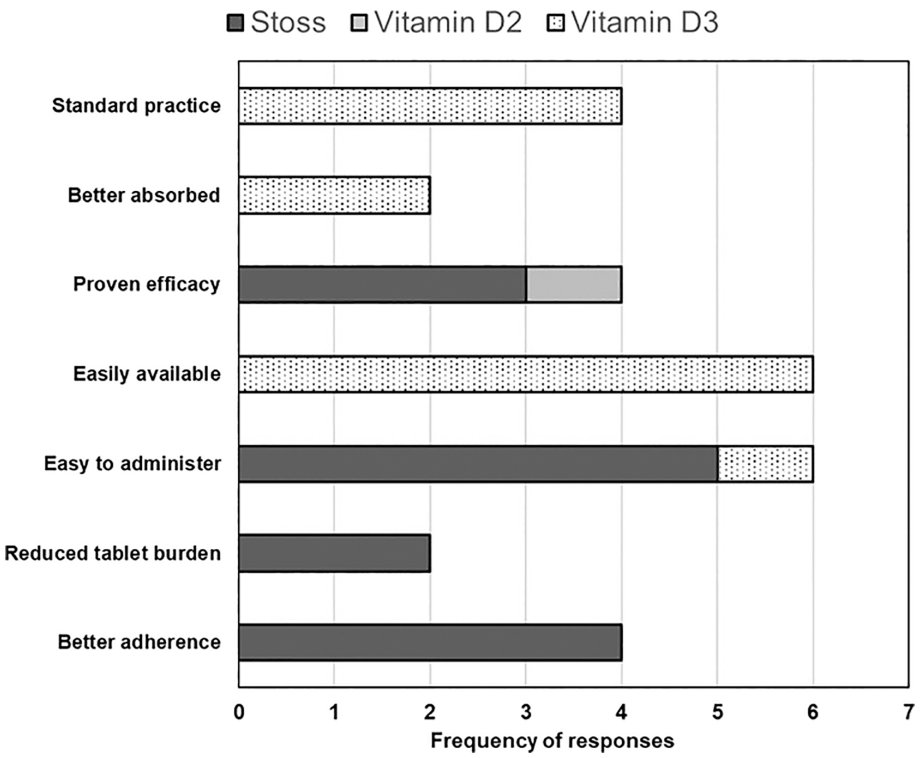

Figure 3 Response frequency related to reasons for choice of particular vitamin D supplementation type. Each bar represents the cumulative number of respondents giving each reason for using a particular type of vitamin D supplementation, color/pattern coded by the type of supplementation used.

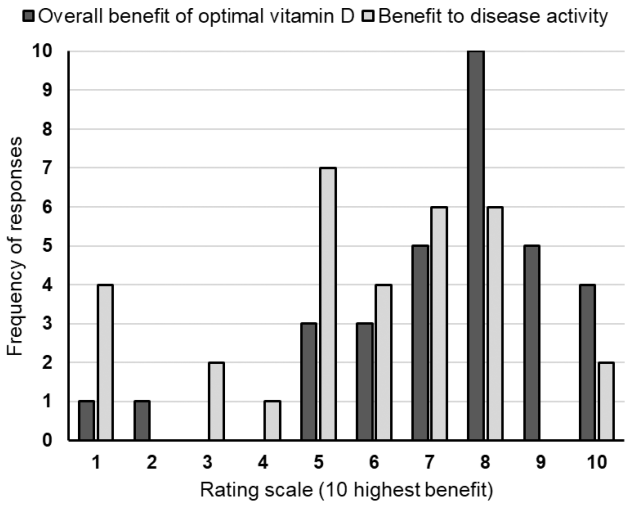

Figure 4 Opinion rating scale of benefit of vitamin D supplementation overall and to disease activity for children with IBD.

treatment is equivocal. While the respondents felt there to be a clear benefit to optimizing vitamin D levels, this was not related to a perceived benefit to disease activity.

The finding in this study that the use of IBD management guidelines did not standardize practice of serum cutoff levels, or dosing regimens, may be a reflection of a number of factors. While a small number of different guidelines were mentioned by respondents, further reading revealed that these do not provide a comprehensive, standardized message with regard to supplementation practices.[14,16,17] The NZ guideline referred to by respondents does not include guidance on optimal levels to be attained or supplementation.[16] The RCH guideline referred to by six respondents is not IBD specific and, although it does include supplementation recommendations, the recommended serum cutoff level for supplementation is lower than recommended for anti-inflammatory benefit for children with IBD (≤75 nmol/L [≤30 ng/mL]).[4,9,17] The ESPGHAN guidelines, referring to children with ulcerative colitis, state concentration cutoffs for supplementation lower than the current recommended level, but do include type and frequency of supplementation.[14] However, ESPGHAN has not provided recommendations in either of their consensus statements for children with CD.[18,19]

Further to these guidelines, other scientific societies have developed evidence-based clinical best practice guidelines to inform vitamin D testing and supplementation for children with IBD. These also do not provide consistent recommendations. The North American Society of Pediatric Gastroenterology, Hepatology and Nutrition recommends measuring serum concentrations if there is significant bone mineral deficit, as well as checking yearly.[13] However, this document does not provide guidance on which specific concentrations should be used as cutoff for supplementation. BSPGHAN has comprehensive recommendations available to their members relating to monitoring, concentration cutoffs, and supplementation at levels lower than currently recommended, but these are not published, nor intended to be used as a guideline.[15] This nonstandardized approach to guidelines may be a reflection of the quantity of evidence available to support definitive statements, as well as the complexity involved in writing and updating guidelines or consensus statements.[20] Few randomized controlled trials (RCTs) are available to support a consensus during guideline development on the best approach, with meta-analyses and systematic reviews also unable to provide agreement on the superiority of any specific supplementation regimen.[21,22]

The low opinion of benefit to disease activity from vitamin D supplementation may be due to previously limited results being available for comparison as not all studies reporting on vitamin D supplementation among children with IBD assess this outcome.[21] Studies among adults with IBD have shown significant benefit of vitamin D supplementation,[23] although it is not always appropriate to extrapolate study findings between the two age groups due to fundamental differences in presentation and disease course.[24,25] However, a recent meta-analysis by Sohouli et al.[22] has provided evidence of benefit to disease activity scores and inflammatory markers from the use of vitamin D supplementation among children with IBD. Awareness of this research and any future new supportive data may result in improved understanding of this topic.

The current study showed that clinicians in NZ test vitamin D seasonally more often than clinicians in Australia. While parts of the North Island of NZ are at a similar latitude to the lower regions of Eastern states of Australia, the exposure to sun required to achieve even one third of their daily dose of vitamin D via skin exposure is far greater during the winter months in parts of NZ than Australia.[26] The latitude where people reside exerts a significant influence on this variable as the skin synthesizes less vitamin D from exposure to sunlight at latitudes 37° north or south of the equator.[2,27] There is an indication of a north–south gradient in the epidemiology of children being diagnosed with IBD with higher prevalence and incidence in Southern regions.[28–30] This disparity in diagnoses according to latitude has specifically been shown among children in NZ.[31] However, only one study carried out in Australia among primary care physicians reported data from which an inference of association may be made toward increased prevalence at lower latitudes, but data were not presented separately for children.[32] With NZ overall having one of the highest global incidence and prevalence rates of pediatric IBD,[31,33] with these numbers increasing,[34] the influence of such factors as latitude may have higher relevance than in Australia where the rates of pediatric IBD may be lower.[33,35]

Strengths. This is the first survey to be carried out among pediatric gastroenterologists throughout Australasia to assess vitamin D testing and supplementation patterns for children with IBD. The response rate was high compared with other survey studies and the distribution of experience and caseload was considered to have provided a representative sample of clinicians. Survey-based research is prone to response bias based on the format of survey questions and the answer options available; however, the risk of this was minimized by having a number of PEDAGREE Executive Committee members review and edit the survey prior to dissemination. In addition, the survey questions for each participant were tailored using branch logic, thereby preventing respondents from answering specific related items if their response indicated it would not be relevant based on their

current practice (e.g. if they did not practice vitamin D testing, then they were not required to answer whether they used guidelines to inform their testing practice).

Limitations. While the response rate was acceptable, additional respondents may have enabled more detailed analysis of the results. Clinicians responding to the survey in Australia were mostly from the Southern regions, thereby limiting additional analysis of, for example, seasonal vitamin D testing. The number of pediatric gastroenterology clinicians based in NZ is small and prevents reporting for that region as a stand-alone commentary, and, as such, the two regions were combined despite the difference in latitude between the two countries that may affect testing/supplementation practices. Sampling bias toward those completing the study having greater interest in the topic, and maybe a greater likelihood of carrying out vitamin D testing/supplementation, may affect the generalizability of the results. While the survey did ask clinicians to report whether their testing/supplementation schedule was influenced by patients having additional risk factors, we did not provide specific guidance on these risk factors and requested free-text feedback as to what these may be. As such, bone mineral density was not specifically mentioned, and the addition of a question regarding this variable would have added valuable insights into the interplay between these clinical testing parameters.

Conclusion

The information presented in this study may be used as an indicator that standardized guidelines for vitamin D testing and supplementation for clinicians caring for children with IBD throughout Australasia are required. The use of the national guidelines by all clinicians in NZ is an encouraging indicator that having tailored guidance may encourage use, despite the lack of standardized approach. In light of the current available guidelines providing conflicting statements on the optimal testing schedule and supplementation regimens, it could be seen that consensus statements developed by Australasian pediatric gastroenterologists may optimize the care of children with IBD in this diverse geographical region.

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