Celiac Disease: An Academy of Nutrition and Dietetics Evidence-Based Nutrition Practice Guideline

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ABSTRACT

Celiac disease is an autoimmune disorder in which the immune system of genetically susceptible individuals elicits a reaction to gluten causing small intestine damage. If left undiagnosed and untreated, the resulting nutrition malabsorption can lead to anemia, bone disease, growth faltering, or other consequences. The condition is lifelong and lacks a cure; the only treatment is lifelong adherence to a gluten-free diet (GFD). This diet is challenging to follow and adversely influences quality of life; however, it is essential to ensure intestinal recovery and prevent future negative health consequences. The Academy of Nutrition and Dietetics convened an expert panel complemented by a celiac disease patient advocate to evaluate evidence for six topics, including medical nutrition therapy; the GFD; oat consumption; micronutrients; pro-/prebiotics; and the low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet. This publication outlines the Academy of Nutrition and Dietetics Evidence Analysis Library methods used to complete the systematic review and guideline development, and summarizes the recommendations and supporting evidence. The guidelines affirm that all individuals with celiac disease should follow a GFD (1C, Imperative) that may include gluten-free oats in adults (2D, Conditional). Children should follow a nutritionally adequate GFD that supports healthy growth and development (Consensus, Imperative) and does not unnecessarily restrict gluten-free oats (Consensus, Conditional). The guidelines indicate nutritional care should include routine nutritional assessment (Consensus, Imperative) and medical nutrition therapy (Consensus, Imperative). At this time, the guidelines do not support a recommendation for the addition of the low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet (2C, Conditional); prebiotic or probiotic supplementation (2D, Conditional); or micronutrient supplementation (in the absence of nutritional deficiency) (Consensus, Conditional). The 2021 Celiac Disease Evidence-Based Nutrition Guideline will assist registered dietitian nutritionists in providing appropriate evidence-based medical nutrition therapy to support people with celiac disease in achieving and maintaining nutritional health and avoiding adverse celiac disease consequences throughout their lives.
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Supplementary materials: *Tables 2 and 3 and the Figure are available at www.jandonline.org*

CELIAC DISEASE IS AN AUTOIMMUNE condition characterized by immune-mediated damage to the small intestine that occurs following gluten consumption in genetically susceptible individuals. The factors that lead to the development of subclinical or overt celiac disease in genetically susceptible individuals are unknown. Once celiac disease manifests, there is no cure and it remains a lifelong medical condition. Currently, the only approved treatment is the total avoidance of gluten that is present in foods, beverages, and medications. Given the ubiquitous nature of gluten in food items in most dietary patterns, total lifelong dietary adherence is challenging for any person living with the condition, as well as those who prepare and share meals with them. Medical nutrition therapy (MNT) provided by a registered dietitian nutritionist or international equivalent (RDN) is needed at celiac disease diagnosis and thereafter to provide support toward achieving and maintaining lifelong dietary adherence to a nutritionally adequate gluten-free diet (GFD).

Ensuring that celiac disease-specific MNT is based on current evidence is critical as our understanding of celiac disease progresses and the nature of a GFD changes. With that in mind, The Academy of Nutrition and Dietetics (Academy) Evidence Analysis Center (EAC) conducted a scoping review (Cheng and colleagues[1]) and a systematic review of the literature to guide the development of evidence-based practice guidelines for individuals diagnosed with celiac disease. This guideline is intended to inform the practice of clinicians working with people diagnosed with celiac disease, including RDNs providing MNT. Like all guidelines, the goal is to provide evidence-based guidance that must be appropriately combined with clinical judgment that best meets the needs of individual patients.

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GUIDELINE OBJECTIVE, SCOPE, AND TARGET USERS

Guideline Objective

The purpose of this guideline was to provide evidence-based recommendations for RDNs delivering MNT to individuals with celiac disease and people who share in their food acquisition, preparation, and consumption. The focus of this guideline was on

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nutrition-related interventions and outcomes that inform nutrition-related practice for people with celiac disease. The primary goals being to promote the achievement and maintenance of optimal health, growth, and development; to prevent and treat celiac disease-associated malabsorption or malnutrition that may lead to comorbidities such as anemia, osteopenia, or osteoporosis; and to improve the quality of life for people following the GFD after celiac disease diagnosis and throughout their lives.

Guideline Scope

The results of the scoping review revealed that existing evidence-based nutrition guidelines for individuals with celiac disease did not focus on MNT or guidelines to help RDNs primarily working with clients in the United States. Therefore, in this new guideline, the expert workgroup panel focused on the effectiveness of the primary nutrition intervention, the GFD, including gluten-free oat consumption and micronutrient supplementation. It also considered newer nutrition interventions utilized in other gastrointestinal conditions as possible adjuvant dietary interventions, including prebiotics/probiotics and the low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (low-FODMAP) diet.

METHODS

Supporting Systematic Review

To inform the current evidence-based practice guidelines, a systematic review was conducted to examine the effectiveness of the primary nutrition intervention, the GFD, along with reconsidering gluten-free oat consumption and micronutrient supplementation and adding adjuvant dietary interventions like prebiotics/probiotics and the low-FODMAP diet. The methods used to conduct the systematic review were the Academy's process[2] and Cochrane Collaborations Grading of Recommendations Assessment, Development and Evaluation (GRADE) methods,[3] with adherence to the standards of Preferred Reporting Items for Systematic Reviews and Meta-analysis checklist.[4] Specific methods for these guidelines and supporting systematic review are briefly described here, with further details available on the Evidence Analysis Library (EAL) website (https://www.andeal.org/).

Systematic Review Process Summary

Question Development, Literature Search, and Study Selection. The questions reviewed in this guideline and supporting systematic review are listed in Table 1. The expert panel followed the EAC process for conducting the systematic review. The population, intervention/exposure, comparison/control, and outcome format for questions, eligibility criteria, and search plan for this systematic review were registered *a priori* on the PROSPERO database[5] (CRD42020169998) (Cheng and colleagues[1]). A comprehensive search of databases, including (MEDLINE (Ovid), Embase (Ovid), Cochrane CENTRAL (Ovid), CINAHL (EBSCO), and Web of Science, PsycINFO) was conducted by a medical librarian. Details of the search plan and search terms are summarized in Table 2 (available at www.jandonline.org). Results of the systematic searches and screening results are presented using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis in the Figure (available at www.jandonline.org).

Study Quality Assessment. Risk of epidemiological bias was considered for each study and was assessed by two independent reviewers using the Quality Criteria Checklist, the Academy's online risk of bias tool. The questions of the Quality Criteria Checklist are based on constructs and risk of bias domains identified by the Cochrane Collaboration, including selection, performance, detection, attrition, and reporting biases. Any discrepancies between the two reviewers were resolved by consensus, and if unable to reach consensus, by including a third independent reviewer.

Table 1. Intervention research question (RQ) list for celiac disease systematic review

Subtopic	Question
MNT[a]/nutrition counseling	**RQ 1:** In patients with celiac disease, how does ***MNT/nutrition counseling*** provided by a RDN[b] or international equivalent, compared with a control, influence nutrition-related outcomes?
Adjuvant prebiotic/probiotic supplementation	**RQ 2:** In patients with celiac disease, what are the effects of ***prebiotics/probiotics***, compared with a control, on nutrition-related outcomes?
Adjuvant low- FODMAP[c] diet	**RQ 3:** In patients with celiac disease, what are the effects of ***low-FODMAP*** diet, compared with a control, on nutrition-related outcomes?
Gluten-free diet	**RQ 4:** In patients with celiac disease, what are the effects of ***gluten-free diet***, compared with a control, on nutrition-related outcomes?
Oat consumption	**RQ 5:** In patients with celiac disease, what are the effects of ***oats***, compared with a control, on nutrition-related outcomes?
Micronutrient supplementation	**RQ 6:** In patients with celiac disease, what are the effects of ***supplements*** (eg, calcium, iron, B vitamins, zinc, copper, multivitamin), compared with a control, on nutrition-related outcomes?

[a]MNT = medical nutrition therapy.
[b]RDN = registered dietitian nutritionist.
[c]FODMAP = fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

Data Synthesis and Grading the Evidence. For all identified outcomes reported in the included studies, a narrative synthesis of evidence was conducted. Due to insufficient and inconsistent data reported for all priori questions/outcomes included, a meta-analysis was unable to be conducted. Instead, conclusion statements were developed for each population, intervention/exposure, comparison/control, and outcome format question and assigned a grade to reflect strength of evidence. GRADE tables were generated for each outcome of interest using GRADEPro and demonstrated how the strength of evidence was derived. Evidence for each outcome of interest was graded as high (A), moderate (B), low (C), or very low (D), as described in Table 3 (available at www.jandonine.org). Study characteristics tables for all included studies and GRADE tables can be found on EAL website (https://www.andeal.org/topic.cfm?menu=5279).

Expert Panel Selection Process. To limit the potential for personal bias or conflicts of interest and to recruit individuals with relevant expertise, the Work Group Selection Subcommittee of the Academy Council on Research followed a transparent process of selecting an expert panel to help provide subject matter clinical and research expertise to conduct the systematic review and develop recommendations. The expert panel consisted of six US-credentialed RDNs with extensive experience in adult and/or pediatric MNT and/or research for individuals with celiac disease. In addition, the parent of an individual with celiac disease served as patient advocate. All expert panel members and the patient advocate participated in each step of the systematic review and guideline development. Supporting members of the team consisted of a research methodologist, a medical librarian, a project manager, a lead analyst, as well as trained evidence analysts. The team had regular virtual meetings to develop research questions, screen studies, analyze evidence, vote and grade conclusion statements, and formulate and discuss recommendations.

Guideline Development. The expert panel followed the EAC and GRADE processes in the development of this guideline. For each systematic review topic, expert panel members completed GRADE's evidence-to-decision (EtD) framework,[6,7] which helps to balance benefits and harms, certainty of evidence, importance of outcomes, resource use, equity, patient values, acceptability and feasibility based on available evidence, and clinical expertise to develop recommendations. In situations where evidence was unavailable to develop recommendations, consensus statements were developed based on clinical expertise and with the goal of achieving better outcomes for clients noting that all clinical practice decisions should be individualized to each specific client. The expert panel voted on approving each recommendation and rated recommendations based on the strength of evidence/confidence in findings and balance of factors considered in EtD framework. For each recommendation, the expert panel and patient advocate provided implementation considerations, potential risks and harms, condition of application, costs, and rationale for the recommendation. Abbreviated supporting evidence for each recommendation is included in this article, with the complete version provided on the EAL website (https://www.andeal.org/topic.cfm?menu=5279).

The grading of the recommendation statements is based on certainty of evidence (ranging from high [A] to very low [D]) as well a clinical expertise and consideration of client values and other EtD framework components. Recommendations rated as Level 1 are strong and generally applicable to majority of the target population. Recommendations rated as Level 2 may be of lower certainty of evidence and are considered weaker recommendations.

External Peer-Review Process. The celiac disease guidelines underwent a peer-reviewed process by an external review performed by 10 people with expertise in providing celiac disease care. These experts used the Appraisal of Guidelines for Research and Evaluation II tool to assess the quality of guideline reporting. Based on the feedback from the external reviewers, the expert panel, patient advocate, and project manager revised the guidelines and accompanying text, and the expert panel voted and unanimously approved all modifications. An executive summary of the recommendations is provided in Table 4.

Guideline Updates. Academy guidelines are reviewed every 5 years when a scoping review is conducted to examine the need for new and revised recommendations based on existing evidence. The Academy Council on Research evaluates and prioritizes research topics based on the results of the scoping reviews and current Academy member needs.

RECOMMENDATION STATEMENTS AND SUPPORTING EVIDENCE

Detailed evidence supporting these recommendations can be found on the EAL website (https://www.andeal.org/topic.cfm?menu=5279&cat=5991).

1. Recommendation for Routine Nutrition Assessment

1.0. In individuals newly diagnosed with celiac disease, it is reasonable that a registered dietitian nutritionist or an international equivalent conduct a comprehensive initial nutrition assessment and evaluates individual ability (including but not limited to access to gluten-free food, socioeconomic barriers, label and menu reading, food preparation, and avoidance of cross-contact skills) and willingness to implement a gluten-free diet, the only available treatment for celiac disease. Follow-up assessments should be individualized according to individual response to treatment, changes in ability or willingness to continue treatment, and signs and symptoms related to celiac disease. ***Rating: Consensus/Imperative***

Rationale

The GFD is the only current treatment for celiac disease. The diet is challenging to implement and for complex social, quality of life, and financial reasons, it is difficult follow; this makes the lifelong burden considerable.[8] Despite the GFD being the only treatment, clear recommendations in terms of the timing, frequency, and duration of nutrition-related and dietary counseling have been vague and inconsistent.[9]

The National Institutes of Health stated that consultation with an RDN is a key element in the management of celiac disease, and "Following initial

Table 4. Executive summary of the Academy of Nutrition and Dietetics Celiac Disease Evidence-Based Nutrition Practice Guidelines

Topic	Recommendation	Recommendation rating
Routine nutrition assessment	In individuals newly diagnosed with celiac disease, it is reasonable that an RDN[a] conduct a comprehensive initial nutrition assessment and evaluate individual ability (including, but not limited to, access to gluten-free food, socioeconomic barriers, label and menu reading, food preparation, and avoidance of cross-contact skills) and willingness to implement a gluten-free diet, the only available treatment for celiac disease. Follow-up assessments should be individualized according to individual response to treatment, changes in ability or willingness to continue treatment, and signs and symptoms related to celiac disease	Consensus Imperative
MNT[b] to improve outcomes	In all individuals with celiac disease, it is reasonable for an RDN to collaborate with individuals with celiac disease, their caregivers and families, and interdisciplinary health care teams to design individualized MNT based on the individual's overall health and nutritional status, personal preferences, psychological and psychosocial factors, and physiological needs. MNT for individuals with celiac disease should focus on comprehensive nutrition assessment and appropriate interventions, including individualized modification of diet, to maintain or improve nutrition status, and monitoring over time	Consensus Imperative
Low-FODMAP[c] Dietary pattern	In adults with celiac disease and abdominal pain, there is insufficient evidence to suggest a low-FODMAP restriction in addition to gluten-free dietary pattern	2 (C) Conditional
Gluten-free dietary pattern Gluten-free dietary pattern for growth and development	For all individuals with celiac disease, the RDN should recommend following a gluten-free diet and support adherence to this diet to improve gastrointestinal health and symptoms, quality of life, quality of dietary intake, maintenance or achievement of a normal body mass index or weight, and improvement in celiac disease-related antibodies and inflammatory, and immunological indicators In children with celiac disease, an RDN should recommend a nutritionally adequate gluten-free dietary pattern to achieve and maintain appropriate growth and development	1 (C) Imperative Consensus Imperative
Inclusion of gluten-free oats (for adults and children)	In adults with celiac disease, an RDN may suggest incorporating gluten-free oats as part of a nutritionally adequate gluten-free diet. In children with celiac disease, gluten-free oats are an appropriate option as part of a nutritionally adequate gluten-free diet.	2 (D) Conditional Consensus Conditional
Addition of micronutrient supplements	For all individuals with celiac disease, it is reasonable for an RDN to advise daily consumption of gluten-free age-, sex- and life stage-appropriate vitamin and mineral supplements if dietary intake and/or laboratory tests suggest nutritional inadequacies	Consensus Conditional
Addition of prebiotic and/or probiotic supplementation	In all individuals with celiac disease following a gluten-free diet, there is insufficient evidence to suggest prebiotics or probiotics supplementation as an adjuvant dietary intervention to the gluten-free diet	2 (D) Conditional

[a]RDN = registered dietitian nutritionist or international equivalent.
[b]MNT = medical nutrition therapy.
[c]FODMAP = fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

diagnosis and treatment, individuals should return for periodic visits with the physician and dietitian to assess symptoms and dietary adherence and monitor for complications. In children, this includes evaluation of growth and development. During these visits, health care providers can reinforce the benefits of adhering to a strict gluten-free diet for life."[10] The British Society of Gastroenterology recommended "Patients with [celiac disease] require follow-up by a dietitian and/or clinician with an interest or expertise in this field (Grade D)," with the grade level indicating this was based on the weak, inconclusive, or inconsistent evidence or expert consensus.[11] The North American Society of Pediatric Gastroenterology Hepatology and Nutrition agreed that "dietary counseling from a dietitian who has expertise in the treatment of [celiac disease] is an essential component of treatment" and in the absence of evidence, recommended annual follow-up with an RDN after symptom resolution and normalization of celiac disease serology.[12] The American College of Gastroenterology guidelines recommended "People with [celiac disease] should be referred to a registered dietitian who is knowledgeable in [celiac disease] in order to receive a thorough nutritional assessment and education on a gluten free diet (Strong recommendation, moderate level of evidence)" but the timing and frequency of counseling were unspecified.[13] The authors do state in their evidence summary that "In addition to providing initial counseling and education, once the relationship with a dietitian is established the patient can be monitored for compliance with the diet and undergo repeated assessments for potential dietary nutrient deficiencies, inadequate fiber intake, and excess weight gain each of which may be associated with adherence to the GFD" and provided a recommendation that "Consultation with a dietitian should be offered if gluten contamination is suspected. (Strong recommendation, moderate level of evidence)."

Encouragingly, the most recent European Society of Paediatric Gastroenterology Hepatology and Nutrition guidelines are clearer, stating "The regular follow-up visits of children with [celiac disease] are preferably carried out by a physician or a dietitian experienced in managing the disease. Local conditions and practices may determine how to apply these recommendations, but self-care treatment without access to adequate health care and dietitians is not recommended. 93% Agreement."[14] Despite acknowledging that "The current literature does not provide evidence on the optimal frequency of follow-up or what should be assessed during visits," European Society of Paediatric Gastroenterology Hepatology and Nutrition recommended "The first follow-up visit should be scheduled 3-6 months after [celiac disease] diagnosis, but with easy access to the celiac service if earlier advice is needed, and sooner review if there are concerns regarding how the family is coping with the diet, if there are ongoing issues with growth or persistent symptoms or a need to repeat blood work earlier. Subsequent visits should be every 6 months until normalization of the [transglutaminase immunoglobulin A] levels, and every 12–24 months thereafter. 93% Agreement." This was followed with a statement that "The assessment of adherence to the GFD is one of the primary goals of [celiac disease] follow-up" and the recommendation that "Since a gold standard method is still missing, adherence to the GFD should be assessed multidimensionally through a careful evaluation of symptoms, dietary interview and/or dietary questionnaires and laboratory tests. 100% Agreement."

In the absence of evidence on routine nutrition assessment, the justification for our expert panel Consensus/Imperative recommendation was drawn from three key bases. First, untreated, newly treated and insufficiently treated celiac disease is associated with intestinal damage that can cause nutrient malabsorption. Second, the symptoms of untreated, newly treated, or insufficiently treated celiac disease are frequently gastrointestinal in nature, and these can negatively influence dietary intake or nutrient utilization. Third, the complexity and difficulty in achieving and maintaining full GFD adherence throughout all life stages and circumstances is well documented. Given these reasons along with the converging consensus recommendations from multiple professional associations, routine nutrition assessment was recommended at celiac disease diagnosis, and follow-up assessments were recommended to be based on individualized assessment of celiac disease management and response to treatment.

2. Recommendation for Gluten-Free Dietary Pattern

2.0. For all individuals with celiac disease, the RDN should recommend following a gluten-free dietary pattern and adherence to this dietary pattern to improve gastrointestinal health and symptoms, quality of life, quality of dietary intake, maintenance or achievement of a normal BMI or weight, and improvement in celiac disease-related antibodies, inflammatory and immunological indicators. ***Rating: Level 1(C)/ Imperative***

2.1. Gluten-Free Dietary Pattern for Growth and Development

In children with celiac disease, the RDN should recommend a nutritionally adequate gluten-free dietary pattern to achieve and maintain appropriate growth and development. ***Rating: Consensus/ Imperative***

Rationale

Type of Evidence Included. The GFD evidence included in this review refers to two different questions: Effectiveness of GFD (a dichotomized analysis of whether the GFD was effective, yes vs no). Given that failure to follow a GFD after confirmed diagnosis is not recommended, this question analyzed evidence evaluating the effectiveness of the GFD in adherents (yes) vs those recently diagnosed and without a history of following GFD (no); or The degree to which the GFD is followed; for example, comparisons of the level of GFD adherence. Data on adherence is limited by key factors, including the self-reported nature of the outcomes (gastrointestinal symptoms) and appropriate comparison groups. This analysis compared levels of adherence despite challenges with comparing adherence levels between studies (eg, lack of consensus definition for low adherence) and in relation to self-reported symptoms.

Effectiveness of GFD. A total of 24 studies were examined that investigated the effect of a GFD compared with a control diet on nutrition-related outcomes in people with celiac disease.

Two randomized controlled trials[15,16] and 22 observational studies[17-37] were included. A total of 12 studies included adults and 12 studies included children or adolescents with celiac disease. All intervention groups investigated, at least in part, the effect of a GFD compared with a control on nutrition-related outcomes.

Effectiveness of Adherence to GFD. A total of 17 unique studies reported in 19 articles that explored the effects of adherence to a GFD on nutrition-related outcomes in people with celiac disease were considered. All studies were observational.[38-54]

Laboratory Measures. The effects of a GFD compared with a control or GFD adherence may not have an effect on select nutrition-related laboratory measures among people with celiac disease. However, certainty of evidence was low. Although five observational studies[21,22,24,31,45] noted improvements in measures, including high-density lipoprotein cholesterol, zinc, serum ferritin, albumin, and hemoglobin with a GFD, one additional observational study[36] and a randomized controlled trial[16] noted no differences in laboratory measures, including high-density lipoprotein cholesterol, hemoglobin, albumin, vitamin B12 and total iron. Results from studies focusing on GFD adherence and nutrition-related laboratory measures indicated that one observational study[45] observed adults with celiac disease and were nonadherent had lower serum ferritin levels than those who were more adherent. This same study, plus an additional observational study[51] with children, noted no differences in other laboratory measures, including glycated hemoglobin level, total protein, calcium, hemoglobin, and albumin.

Dietary Intake. There is a possible positive effect of a GFD compared with a control diet on dietary intakes among people with celiac disease, but the positive effect was not seen with differential GFD adherence levels. One study in children demonstrated that those who followed a GFD consumed fewer saturated fatty acids than those on a gluten-containing diet.[21] An additional study among adolescents showed that those on a GFD consumed more vegetables, poultry, and bread than those on a gluten-containing diet.[25] This review indicated that there is no evidence to suggest that adherence to a GFD influences dietary calcium or total energy intake among children with celiac disease.[38,51]

Weight/Body Mass Index. The effect of a GFD and GFD adherence may influence the maintenance and achievement of a normal body mass index (BMI) or weight, although the certainty of evidence was low. Two studies,[21,30] both with children and one study with adults[31] with celiac disease noted improvements in either weight or BMI among groups that were following a GFD when compared with a control. Five studies noted no difference in either BMI or weight.[16,25,26,28,32] A similar pattern was observed for GFD adherence. One study in children showed lower BMI values (trending toward underweight) among those following a strict GFD in comparison to those with frequent nonadherence.[53] Another study showed that children who adhered to a GFD experienced increases in BMI (trending toward a normal BMI) in comparison to those who were nonadherent.[54] In a study with adults, compliance with a GFD was associated with a lower BMI (that was still in the normal category) in comparison to those with poor adherence whose mean BMI was in the overweight category.[44] Four additional observational studies noted no difference in BMI between adherence groups.[40-42,51]

Quality of Life. The evidence suggests that a GFD compared with a control or greater GFD adherence may improve quality of life indicators among people with celiac disease; however, the certainty of evidence is very low. Three studies in adults[16,19,31] and one study in children[33] suggest that a GFD compared with a control group may have a positive influence on quality of life. The effect of GFD adherence on indicators of quality of life among children and adults with celiac disease was mixed. There was conflicting observational evidence on the role a GFD in improving measures of quality of life, with four studies noting improvement in quality of life measures with greater GFD adherence[39,50,53] and five studies[43,46,48,49,52] noting no difference between groups.

Indicators of Gastrointestinal Health and Symptoms. A GFD compared with a control may lead to an improvement of indicators of gastrointestinal health and gastrointestinal symptoms among people with celiac disease; however, there was limited current evidence to suggest the same for GFD adherence where the certainty of evidence was low. Six studies in adults[15,16,19,27,31,36] and two studies in children[17,27] noted improvements in gastrointestinal symptoms and indicators of gastrointestinal health with a GFD. Two studies[18,35] noted no evidence of an association between diet and gastrointestinal health. Although Laine and colleagues,[28] Koskinen and colleagues,[27] and Korpimaki and colleagues[26] also assessed markers of gastrointestinal health, between-group significance was unreported. There is limited current evidence to suggest that adherence to a GFD influences indicators of gastrointestinal health and gastrointestinal symptoms among people with celiac disease. Whereas one observational study[47] noted improvements among adults in self-reported gastrointestinal symptoms with adherence to a GFD, four other studies[42,44,50,55] in adults provided no evidence of an association between adherence and gastrointestinal symptoms.

Bone Metabolism. The evidence on the effect of a GFD compared with a control on indicators of bone metabolism was inconclusive. Adherence to a GFD had a positive influence on bone mineral density in children with celiac disease, although the certainty of evidence was low. Three observational studies (two with children and one with adults) found that groups that followed a GFD had higher bone mineral density than the control group,[29,30,37] whereas one observational study[45] with adults and one randomized controlled trial[16] with adults found no evidence of difference between. Adherence to a GFD may have a positive effect on indicators on bone metabolism among people with celiac disease. Four observational studies in children found that those who adhered to a GFD had higher bone mineral density than groups with poor adherence.[38,41,51,56]

Celiac disease-related antibodies, and inflammatory and immunological indicators. A GFD and GFD adherence are associated with improved celiac disease-related antibodies, and inflammatory or immunological indicators among people with celiac disease; however, certainty of evidence was low. A GFD compared with a control diet had a positive effect on celiac disease-related antibodies and inflammatory or immunological indicators among people with celiac disease. Five studies concluded that a GFD resulted in improvement in markers of antibodies and inflammation compared with a control.[15,16,27,36,45] Adherence to a GFD had a potential effect on celiac disease-related antibodies and inflammatory or immunological indicators among people with celiac disease. Hopman and colleagues,[42] Kahramanoglu and colleagues,[45] and Wagner and colleagues[53] all reported on the influence of adherence to a GFD on celiac disease-related antibodies. All three studies noted a significant difference in antigliadin antibodies between groups with varying adherence. Hopman and colleagues[42] noted a significant difference in the number of adults with positive immunoglobulin A-endomysial between groups who followed a strict GFD in comparison to those who followed a nonstrict or no GFD, with the fewest number in the strict GFD group. Kahramanoglu and colleagues[45] concluded that thymic stromal lymphopoietin, immunoglobulin A antibodies to tissue transglutaminase and immunoglobulin G antibodies to tissue transglutaminase levels were significantly higher in the nonadherent group of adults in comparison to the adherent group.[45] Finally, Wagner and colleagues[53] reported that among adolescents with varying levels of GFD adherence, there were more positive anti-gliadin antibody cases at the last blood checkup in people with frequent nonadherence than in people who were fully adherent to the GFD.

3. Gluten-Free Oats

3.0. Celiac Disease (CD): Inclusion of Gluten-free Oats: Adult

In adults with celiac disease, the RDN may suggest incorporating gluten-free oats as part of a nutritionally adequate GFD. ***Rating: Level 2(D)/Conditional***

3.1. CD: Inclusion of Gluten-free Oats: Children

In children with celiac disease, the RDN may suggest incorporating gluten-free oats as part of a nutritionally adequate GFD. ***Rating: Consensus/Conditional***

Rationale

Until recently, people with celiac disease were frequently cautioned to avoid consumption of oats as part of a GFD despite a lack of consensus for this clinical advice.[57,58] The rationale was based on inconsistent clinical evidence reporting sensitivity to oat protein consumption among some people with celiac disease. Uncertainty existed as to whether the apparent sensitivity was due to a true dietary intolerance to pure oats in a subgroup of individuals with celiac disease with no other explanatory causes of sensitivities, to cross-reactivity associated with certain oat cultivars possessing immunoreactive avenin epitopes, and/or to actual cross-contamination of oats or oat-containing food products with cereal grains containing gluten, including wheat, barley, or rye.[59-61]

The systematic review included only two studies that specifically stated purified gluten-free oats (vs unspecified purity oats) were evaluated.[62-64] Despite this lack of distinction regarding the purity of oats, the systematic review results indicated no differences in immunoreactivity/toxicity as assessed by celiac disease-specific antibodies, intraepithelial lymphocytes, and oat-specific (avenin, gliadin) antibodies outcomes.[63-69] Histological evidence revealed there were no differences in villous height to crypt ratio[64] or improvements in mucosal villous crypt depth ratios.[67] People who consumed oats did not self-report any differences in gastrointestinal symptoms using the Gastrointestinal Symptom Rating Scale[62,63,65] and one study observed improved Gastrointestinal Symptom Rating Scale scores[67] with daily oat consumption.

Consuming the recommended amount of fiber from whole grains is a challenge for many Americans, both with and without celiac disease.[70,71] Oats contain soluble fiber and dietary quality was improved with significantly higher fiber intake[67,72] whereas one study observed lower plasma total cholesterol and alanine aminotransferase.[72] Løvik and colleagues[72] observed reductions in total protein, albumin, folate, and phosphorus and greater aspartate aminotransferase and bilirubin levels. The systematic review indicated that liberalizing the GFD to include oats did not negatively influence quality of life indicators associated with psychological well-being and improvements in physical scores (limitations due to physical health problems, pain, or general health) and general well-being were evident.[65] Although consuming oats did not alter self-reported GFD adherence among highly adherent adults (≥96.5% adherence),[65] a reduction in gluten intake was observed.[72] Lastly, oat consumption was not associated with differences in BMI in adults[67] or children.[63]

4. MNT to Improve Outcomes

4.0. In all individuals with celiac disease, it is reasonable for a RDN to collaborate with individuals with celiac disease, their families, and interdisciplinary healthcare teams to design individualized MNT based upon the individual's overall health and nutritional status, personal preferences, psychological and psychosocial factors, and physiological needs. MNT for individuals with celiac disease should focus on comprehensive nutrition assessment and appropriate interventions, including individualized modification of diet, to maintain or improve nutrition status, and monitoring over time. ***Rating: Consensus/Imperative***

Rationale

A total of eight studies were examined that explored the effects of MNT compared with a control on nutrition-related outcomes in people with celiac disease. Three neutral-quality randomized controlled trials,[73-75] three neutral-quality cross-sectional studies,[20,76,77] and two neutral quality cohort studies[31,78] were included.

The effects of MNT compared with a control on nutrition-related laboratory measures among people with celiac disease were inconclusive. One prospective cohort study[31] concluded that there was a significant improvement in mean hemoglobin and serum albumin levels among both groups who received dietary counseling by a RDN;

however, one group received one more counseling session making equivalent comparisons difficult.

The effect of MNT on anthropometric characteristics among people with celiac disease in comparison to a control was still unclear. One prospective cohort study[31] and a cross-sectional study,[20] indicated an improvement in BMI and weight status after receiving nutrition counseling from an RDN, whereas, another cross-sectional study[76] concluded that there was no significant difference in BMI between people with celiac disease who had received treatment from an RDN and people who did not. Cheng and colleagues[20] found that the length of follow-up with an RDN was associated with BMI. Moreover, among the underweight groups, there was a beneficial association between greater follow-up years and increases in BMI. In addition, Rajpoot and colleagues[31] concluded that both treatment-naïve and follow-up groups that received nutrition counseling from an RDN experienced a significant improvement in weight from baseline to 6 months.

Evidence on the effect of MNT on indicators of quality of life among people with celiac disease in comparison to a control was mixed. Out of the four studies that reported on the outcome of quality of life, two studies[31,74] indicated significant improvements in quality or life after receiving MNT from an RDN. However, two other studies indicated no effect of MNT on quality of life.[75,76]

There was mixed evidence on the effect of MNT on GFD adherence among people with celiac disease in comparison to a control. Two studies indicated that people who took part in nutrition counseling by an RDN reported significant improvements in GFD adherence rates compared with those who did not.[31,75] On the other hand, Mahadev and colleagues[76] found that RDN counseling was not associated with dietary adherence.[76] Two other studies that compared effect of a provider (dietitian or physician) on dietary compliance among people with celiac disease indicated that dietary compliance was similar, regardless of which professional provided MNT.

Out of the three studies that reported on effect of MNT on indicators of gastrointestinal health and gastrointestinal symptoms among people with celiac disease, two studies observed significant improvements in gastrointestinal symptoms.[31,74] However, Mahadev and colleagues[76] found that involving an RDN was not associated with celiac disease symptoms.

5. FODMAP Dietary Patterns

5.0. CD: FODMAP Dietary Pattern

There is insufficient evidence to suggest adults with celiac disease and persistent gastrointestinal symptoms follow a low-FODMAP dietary pattern in addition to a GFD. ***Rating: Level 2(C)/ Conditional***

Rationale

Individuals diagnosed with celiac disease who follow a strict GFD are anticipated to experience recovery, including intestinal mucosal repair and resolution of autoimmune responses associated with gluten exposure. However, there is a small group of individuals with nonresponsive celiac disease or refractory celiac disease that, despite apparent adherence to a GFD, continue to experience persistent gastrointestinal symptoms resembling irritable bowel syndrome (IBS) associated with a diminished quality of life.[79] Currently, there are no additional nutrition recommendations or guidelines for treating people with celiac disease and persistent gastrointestinal symptoms after gluten exposure has been eliminated.

The low-FODMAP dietary pattern that restricts fermentable oligo-, di-, and monosaccharides and polyols has been shown to be beneficial among some people managing IBS symptoms and a dietary trial was suggested as part of IBS interventions.[80-82] Despite shared clinical, client, and commercial interest in the low-FODMAP diet, the number of research studies investigating the low-FODMAP diet in people with only celiac disease who do not have IBS or other comorbidities is very limited. Indeed, the systematic review results were based on one small randomized clinical trial among Italian adults who had been following a GFD for at least one year but continued to experience gastrointestinal symptoms.[83] After consuming a low-FODMAP diet for a minimum of 21 days, quality of life indicators, self-reported gastrointestinal symptoms, and indicators of gastrointestinal health were not different between the intervention and control groups. Only a reduction in abdominal pain was observed in the low-FODMAP intervention group. Given the considerable interest in the low-FODMAP diet, it may be possible in the future to extract data from recently published studies such as the one by van Megen and colleagues[79] that included a subgroup of participants with celiac disease only (vs celiac disease and IBS or other comorbidities).

6. Vitamins and Mineral Supplements

6.0. CD: Addition of Vitamin and Mineral Supplements

For all individuals with celiac disease, it is reasonable for the RDN or international equivalent to advise daily consumption of gluten-free age-and sex-appropriate vitamin and mineral supplements if dietary intake and/or laboratory tests indicate nutritional inadequacies. ***Rating: Consensus/Conditional***

Rationale

Comorbidities such as anemia, osteopenia, and osteoporosis, and among children, impaired growth and development, may be the first sign of undiagnosed celiac disease. In people with recently diagnosed celiac disease or with nonresponsive celiac disease or refractory celiac disease who experience unresolved intestinal damage and an associated inflammatory immune response, ongoing nutrient malabsorption and altered nutrient metabolism associated with disease processes may continue. Even with disease remission and full intestinal healing, consuming a GFD has been associated with concern for sufficient nutritional intake and/or biomarker concentrations of iron (or ferritin), folate, vitamin B12, vitamin D, calcium, zinc, selenium, and magnesium.[71,84–87] Furthermore, depending on individual food choices, the differences in mandatory food fortification and enrichment policies between gluten-free and their standard gluten-containing counterparts differ. This can influence staple cereal-based foods (eg, pasta, bread, and cereals) and flours that are rich sources of iron, folate, niacin, thiamin, riboflavin, and calcium.[84,86]

This recommendation is aligned with general MNT guidance whereby people who are at risk of nutritional deficiency as a result of RDN-assessed dietary intake inadequacies or laboratory biomarkers of nutritional status should consider consuming an appropriate micronutrient supplement. The systematic review results supporting this recommendation in the context of specific celiac disease-associated risk was inconsistent and limited across key nutrients of interest. For example, while zinc supplementation increased biomarkers of zinc status in one trial providing 2 mg zinc/kg/day to children,[88] the other providing 20 mg elemental zinc in children found no differences.[89] The systematic review was also inconsistent among adults with unspecified baseline micronutrient status. In adults taking daily multivitamins with vitamin B6, folate, and vitamin B12, significantly higher serum vitamin B6, folate, and vitamin B12, and lower total homocysteine levels were observed, although no differences in mucosal villus atrophy was reported.[90] In contrast, in adults taking daily supplements containing 0.8 mg folic acid, 0.5 mg cyanocobalamin, and 3 mg pyridoxine, only total homocysteine was significantly lower, whereas serum B12, folate, hemoglobin, creatinine, and plasma pyridoxal 5'-phosphate levels and erythrocyte mean corpuscular volume were not different.[90] Daily L-carnitine (2 g) supplementation favorably influenced self-reported fatigue in adults with unspecified L-carnitine status at baseline.[91] In contrast, micronutrient supplementation did not influence pediatric weight gain (zinc supplement),[88] quality of life (as measured by Short Form-36 General Health Perception Scale and EuroQoL) or asthenia (L-carnitine supplement)[91] or well-being (as measured by the Psychological Well-Being Index) (folic acid, vitamin B12, and vitamin B6 supplement).[92] Overall, until the body of evidence begins to coalesce around common nutrients of interest (including dosages, nutrient/vitamer types, and duration of intervention), populations (including pediatric, adult, confirmed absence or presence of baseline nutritional deficiencies, newly diagnosed or long-term disease, and those with confirmed signs and symptoms of celiac disease in remission or persisting) and outcomes of interest (markers of bone health, growth anthropometrics, differentiation between iron deficiency anemia vs anemia of inflammation, and biomarkers of nutritional status), the systematic review process and resulting recommendations specific to celiac disease will remain a challenge.

7. Prebiotics or Probiotics Supplementation

7.0. CD: Prebiotics or Probiotics Supplementation

In all individuals living with celiac disease and following a gluten-free diet, there is insufficient current evidence to suggest adding prebiotics or probiotics supplementation. ***Rating: Level 2(D)/Conditional***

Rationale

Intestinal dysbiosis characterized by a reduction in microbiota biodiversity, numbers, and a relative imbalance between beneficial and pathogenic or proinflammatory microbes such as gram-negative bacterial genera like *Bacteroides*, *Prevotella*, and *Escherichia* has been observed in people with celiac disease and may contribute to celiac disease pathogenesis.[93–95] It has also been reported that some degree of intestinal microbial difference persists even after initiation of a GFD.[93] In an effort to restore this microbial imbalance and minimize any functional consequences, adjuvant therapeutic prebiotic/probiotic intervention strategies have focused on direct administration of live microorganisms, primarily *Bifidobacterium* and/or *Lactobacillus* species, through the consumption of probiotic supplements (in capsule, tablet, powder, or sachet forms) and in foods enriched with live probiotic cultures; or indirect support for the growth or activity of beneficial microbes via the consumption of prebiotics (eg, oligofructose-enriched inulin, lactulose, and lactobionic acid) in naturally rich or enriched foods.[94,96]

Despite the systematic review considering a wide variety of subjective (quality of life[97] and gastrointestinal symptoms[97–99]) and objective (anthropometrics,[98,100] biomarkers of nutritional status,[101–103] bone metabolism,[100] celiac disease-related immunological indicators,[98–100,103] intestinal microbiome,[97,98] fecal microbiome,[97,104–106] intestinal physiology,[107] or fecal short-chain fatty acids concentration[104]) outcomes, the evidence was inconclusive. Thus, the systematic review did not support the recommendation of adjuvant prebiotic/probiotic dietary interventions in addition to the GFD.

A challenge when considering prebiotic and probiotic evidence is that there is no consensus prebiotic or probiotic formulation for microbial composition, dosage, or duration to compare across studies. When this is combined with the large number of possible outcomes (eg, intestinal vs fecal microbiome; composition vs number vs function of individual microbes or the entire microbial community; gastrointestinal histology vs mucosal immune markers vs subjective reporting of gastrointestinal symptoms that may overlap with other comorbidities unrelated to celiac disease), a much larger body of homogenous evidence will be required to justify moving toward a conclusive recommendation for adjuvant prebiotic/probiotic supplementation.

BENEFITS, HARMS, AND COSTS OF IMPLEMENTING RECOMMENDATIONS

The expert panel concluded that the benefits of the GFD in treatment for celiac disease outweigh potential harms. No significant adverse effects were reported from interventions on outcomes of interest. Limited evidence on interventions indicated improvements in nearly all outcomes of interest. The expert panel acknowledges that in some people implementation of these recommendations may have potential risks and unintended harms; thus, individualizing implementation of recommendations and monitoring clients is important.

The gluten-free dietary pattern does not eliminate any food group; however, the extent that gluten is naturally occurring in wheat, rye, barley, and triticale or incorporated into processed foods intentionally (eg, an added ingredient) or unintentionally (eg, cross-contact through the manufacturing or production processes) is widespread. The individual dietary choices associated with implementing a GFD may increase the risk of nutritional inadequacy for some individuals, especially for those with insufficient nutrition-related

literacy. Supplementation must be considered on an individual basis and assessment of risk of nutritional deficiencies. Individuals supplemented with micronutrients should be monitored regularly to determine the ongoing justification for supplementation and to ensure supplementation dosages are appropriate.

Potential costs associated with implementing these recommendations may include consultation costs with RDNs. The direct cost to the individual for initial and follow-up consultations varies according to health insurance coverage and may be a barrier for some. Although a GFD is possible to follow on any food budget, the additional financial cost of gluten-free versions of staple foods (eg, bread, certified gluten-free flours, oats, and others) and gluten-free versions of time-saving common convenience foods (eg, deli, frozen, canned, and packaged foods) can be financially burdensome for some individuals. Although the consumer marketplace for gluten-free foods has expanded in recent years, physical access to gluten-free foods is not universal throughout the United States and the additional costs of shipping gluten-free versions may be important to consider when estimating the overall costs associated with implementing a GFD.

MNT-associated costs are markedly less than the costs associated with celiac disease complications that may result from nonadherence to a strict GFD. However, social determinants of health, including access to an RDN, insurance reimbursement, food access, and economic stability can lead to suboptimal quality of care and consequently, health inequities, and disparities.

IMPLEMENTATION CONSIDERATIONS

The expert panel encourages individualizing MNT approaches as appropriate for each patient or client based on clinical judgment and appropriate factors, including but not limited to health-related history, diet preferences, culture, food access and security, and socioeconomic status. When implementing these recommendations, RDNs should consider, respect, and incorporate principles of inclusion, diversity, equity, access, and social determinants of health in their MNT approach. For example, in cases of individuals or clients residing in rural areas or with decreased access to insurance or challenges with transportation to medical care, RDNs should consider the feasibility of telephone or virtual appointments when appropriate.

The celiac disease evidence-based nutrition practice guideline should be acceptable and feasible for RDNs to implement because the GFD is the only treatment option for individuals with celiac disease. The role of RDNs in management of celiac disease is very important. The expert panel was unable to provide a specific number of required consultations with RDNs based on the currently available evidence. However, guidance from multiple health and professional organizations recommend that once a person is diagnosed with celiac disease, an RDN visit is important, with follow-up visits strongly encouraged.

RDNs should assess the needs of clients and prepare a client-centric nutrition care plan. RDNs should educate and discuss the importance of GFD and provide resources to help improve adherence to GFD. RDNs should educate and provide resources to help develop good quality knowledge of food budgeting/purchasing practices, food preparation skills and equipment, combined with the motivation to prepare meals at home, the GFD can be comparable in financial cost. For individuals interested in also following the low-FODMAP dietary pattern, RDNs should share client education resources on the low-FODMAP diet plan, but it should be noted that the resources target people with IBS and not those with celiac disease plus coexisting IBS. Resources describing the low-FODMAP dietary pattern are available from The Celiac Disease Foundation (https://celiac.org/fodmaps-and-celiac-disease/) and Monash University (https://www.monashfodmap.com/).

Individuals with recently diagnosed celiac disease may be at greater risk of nutritional deficiencies as a result of celiac disease pathology and intestinal epithelial damage impairing nutrient absorption or the immune activation associated with inflammation that alters nutrient metabolism (eg, altered iron absorption due to intestinal damage and inflammation-impaired iron absorption and metabolism). RDNs should work with the multidisciplinary health care team to consider the current extent of intestinal damage during the recovery period and beyond.

RDNs should be aware that due to different mandatory nutrient fortification or enrichment policies for gluten-free flours and processed foods that are country-specific, some gluten-free foods are not nutritionally equivalent to their standard gluten-containing counterparts (eg, enriched wheat flour and ready-to-eat cereals). RDNs should be familiar with the client dietary history and the nutrient composition of gluten-free foods that are consumed when evaluating the nutritional adequacy of gluten-free dietary intakes. For those at risk of nutritional insufficiency based on an RDN's estimated dietary intake and/or due to the current signs and symptoms associated with malnutrition, malabsorption, or other disease processes based on consultation with the health care team, RDNs should consider recommending an age-, sex- and life stage (eg, pregnancy, lactation, and growth) appropriate vitamin or mineral supplement for individual clients. RDNs should evaluate the justification for ongoing vitamin or mineral supplementation at follow-up visits. For some clients, RDNs will need to consider the economic burden of nonprescription vitamins or minerals in their recommendations and risk–benefit analyses. When given the opportunity, all RDNs should counsel and support clients to consume a nutrient-dense GFD that adheres to the 2020-2025 Dietary Guidelines for Americans (https://www.dietaryguidelines.gov/) and MyPlate (https://www.myplate.gov/) recommendations.

To support clients accessing government-supported food assistance programs such as the Supplemental Nutrition Assistance Program, RDNs should counsel that gluten-free oats can be included as part of the allowable purchases. For clients who access community and/or school-based food pantries, RDNs can advocate for food pantry administrators to accommodate the medical need for gluten-free oats and food items as part of celiac-disease appropriate food baskets and food donations.

People with celiac disease may be interested in initiating or may already be using prebiotics/probiotics. RDNs

should have a working knowledge of the current definitions of prebiotics and probiotics, foods with natural or added prebiotics/probiotics, and counseling strategies to discuss the evaluation of marketing claims and relevance to celiac disease (vs other similar, but distinct medical conditions like IBS) during both initial recovery that follows a recent celiac disease diagnosis and during long-term celiac disease management.

The Academy provides a general (nonceliac disease-specific) resource on probiotics (https://www.eatrightpro.org/news-center/nutrition-trends/foods-and-supplements/probiotics), with additional information provided in the National Institutes of Health health professional fact sheet on probiotics (https://ods.od.nih.gov/factsheets/Probiotics-HealthProfessional/). The Food and Drug Administration summarizes regulatory policies of food and diet products and health claims (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/complementary-and-alternative-medicine-products-and-their-regulation-food-and-drug-administration). Notices summarizing the status of individual prebiotics are typically issued as generally recognized as safe notices that can be accessed by searching the Food and Drug Administration website and specific prebiotic name. Another resource is the International Scientific Association of Probiotics and Prebiotics, which represents an association of academic and industrial scientists involved in basic and applied research on probiotics and prebiotics and provides health professional and consumer resources. RDNs should also be aware of the additional expense of prebiotics/probiotics that may not be covered by health insurance, and be prepared to discuss the additional cost burden for clients who are experiencing economic challenges.

Strengths and Limitations

Key strengths of this celiac disease evidence-based guideline include the quality of the rigorously conducted systematic review and the use of an EtD framework to translate evidence into recommendations. Another strength was that all stages of the systematic review and guideline development were informed by the collaborative efforts of the expert panel and a celiac disease patient advocate. The perspectives of patient advocates are particularly important in the context of celiac disease because the only available therapeutic intervention is a strict GFD that must be followed throughout all life stages and socioeconomic circumstances, and because the needs of one person with celiac disease influences an entire household that often follows the same diet (to minimize inadvertent cross-contamination in home kitchens or for practical reasons to avoid the need to purchase, prepare, and monitor gluten-free and non–gluten-free ingredients, meals, and snacks within a single household). Finally, strengths include the reexamination of prior Academy guidelines on oat consumption in light of new evidence that has shifted to support greater liberalization of the GFD; an expansion of guidelines to include the first Academy guideline on the low-FODMAP diet in celiac disease; and an evaluation of prebiotic/probiotic supplementation as an adjuvant nutritional intervention to the GFD in the context of celiac disease.

Because the GFD is the only therapeutic intervention for people diagnosed with celiac disease, the quality and availability of the evidence for some questions was influenced by the inability to randomize to a placebo (eg, non–gluten-free) diet or to blind providers and participants to the assigned treatment group (eg, intervention or control). Other limitations included considerable variation in the definition of the exposure (eg, micronutrient or prebiotic/probiotic formulation; pure gluten-free oats vs unspecified oats), the population (eg, children, adults, newly vs long-term diagnosed, symptomatic or asymptomatic, and presence of comorbidities or otherwise) and outcome measures (dietary intake, biomarkers of nutritional status, anthropometric characteristics, quality of life, and symptoms scoring systems). As a result of these evidence limitations, the expert panel developed some guidelines based on consensus aligned with biological plausibility, clinical experience, and literature outside of the scope of the systematic review (eg, routine nutrition assessment and oat consumption in children with celiac disease). Lastly, health care professionals experienced in adult and pediatric celiac disease management participated in the expert panel; however, gastroenterologists were invited but did not volunteer to participate.

FUTURE RESEARCH

Exciting areas of future research include identifying tolerable dietary gluten exposures in combination with novel pharmacological interventions that are in development and designed to mitigate unintentional (or perhaps even some degree of intentional) gluten exposure or to reduce symptoms among those with nonresponsive or refractory celiac disease such as larazotide acetate (AT-1001, currently in Phase III trials), latiglutenase (IMGX-003, formerly known as ALV003, Phase IIb), and PRV-015 (Phase IIa)[108,109]; ongoing efforts to ascertain the safety and efficacy of dietary adjuvant therapies that may include prebiotics/probiotics or other dietary supplements, dietary patterns (eg, low-FODMAP diet or others) or functional foods that promote a beneficial gastrointestinal microbiome in people with celiac disease.[79,110] This area of research will benefit considerably from advances in other disciplines that promote a greater understanding of the human microbiome and its functional implications in health and disease, and the development of the scientific and statistical methodologies needed to move forward to understanding complex diet and microbiome interactions; accurately identifying and/or quantifying actual gluten-exposure through point-of-consumption consumer testing tools (eg, portable antibody-based assays to rapidly detect proteins in food) or other sensors[111] that may reduce misclassification of study participants according to actual gluten-exposure; and the role and timing of early gluten exposures and the GFD or other dietary factors (eg, those influencing the intestinal microbiome) in preventing celiac disease among people at genetic risk of developing the disease.[112]

CONCLUSIONS

These guidelines support the clinical practice of implementing a lifelong, strict GFD as the sole therapeutic intervention for people diagnosed with celiac disease. The guidelines also now support the liberalization of this diet to include gluten-free oat consumption. The guidelines continue to affirm the

important role of RDNs in providing individualized MNT to give people with celiac disease the greatest chance of achieving and maintaining dietary and health success. Although there are no inherent nutritional inadequacies associated with a GFD, there is a complex interplay between individual food choices, dietary avoidance patterns, socioeconomic challenges, nutrition literacy, culinary skills, altered nutrient composition due to differing food fortification and enrichment policies, and an increased risk of suboptimal nutritional status associated with intestinal damage and disease recovery processes or among those with lower dietary adherence or disease remission. Thus, these guidelines continue to support the rationale for RDNs to provide routine individualized nutrition assessment to people recently diagnosed and to those who have been living with celiac disease for longer periods. Although the guidelines do not support micronutrient supplementation in otherwise nutritionally replete individuals with celiac disease, if an individual is evaluated by an RDN to be at risk of dietary inadequacy or nutritional deficiencies or confirmed to be nutritionally deficient, then micronutrient repletion would be part of the nutrition-related standard of care. The evidence base for the low-FODMAP diet and prebiotic/probiotic supplementation is expanding, but as of the date of this systematic review and guideline development, there was insufficient evidence or consensus opinion to support a recommendation to implement either as adjuvant nutrition interventions in celiac disease.

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

During the development of this guideline, the patient advocate, M. Gellar, was employed by The Celiac Foundation and as part of her employment she has consulted for ICON, Schar, and Takeda, and received meeting expenses from Schar, Prevention, and Bio.

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AUTHOR CONTRIBUTIONS

J. McDermid, A. Almond, K. Roberts, T. Taylor, E. Germer, and M. Geller served as content experts on the expert panel. D. Handu served as the project manager and lead analyst. All authors worked together to design and interpret systematic reviews and develop the guideline. J. McDermid and D. Handu wrote the first draft of the manuscript with contributions from all co-authors. All authors reviewed and commented on subsequent drafts of the manuscript and approved the final version.

Table 2. Celiac disease systematic review search plan

	Include	Exclude
Age	**All RQs**[a]**:** Infants, children, and adolescents (0-17 y) and adults (≥18 y)	**All RQs:** None
Settings	**All RQs:** Any	**All RQs:** None
Health status	**All RQs:** People diagnosed with celiac disease according to the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition or the 2012 European Society for Pediatric Gastroenterology, Hepatology, and Nutrition diagnostic criteria	**All RQs:** Undiagnosed, at-risk, or self-reported celiac disease diagnoses
Nutrition-related problem or condition	**All RQs:** Diabetes mellitus (type 1); osteoporosis; infertility; lymphoma; irritable bowel syndrome; thyroid disease; peripheral neuropathy; Down syndrome; Turner syndrome; dementia; hepatitis; epilepsy; Graves' disease; cirrhosis; psoriasis; autism; nonresponsive celiac disease; dermatitis herpetiformis; obesity	**All RQs:** None
Interventions/ exposures	**RQs 1-6:** Nutrition intervention, including MNT[b] provided by RDN[c] (RQ 1), use of prebiotics/probiotics (RQ 2), low-FODMAP[d] diet (RQ 3), GFD[e] (RQ 4), oat consumption (RQ 5), micronutrient supplements (eg, calcium, iron, B vitamins, zinc, copper, multivitamin) (RQ 6)	**RQ 1:** A nutrition intervention not implemented by RDN **RQs 2-6:** Other/no nutrition intervention
Comparison	**RQs 1-3, 5-6**: Placebo or no treatment (eg, minimally active intervention, such as printed materials) **RQ 4:** Control (eg, people without celiac disease, established recommendation/level)	**RQs 1-3, 5-6**: No placebo or active interventions **RQ 4:** No control or active interventions (eg, GFD + probiotics)
Outcome — intermediate outcomes/ biological effects, clinical outcomes (Timing/follow-up)	**RQs 1-6:** • Anthropometrics/growth: Length/height-for-age, BMI[f] • Bone health: DEXA[g] scan • Nutritional status: complete blood count, comprehensive metabolic panel, iron profile, lipid, thyroid function, red blood cell folate, vitamin B12, vitamin D, zinc • Gastrointestinal health/symptom: CDSD[h], CDAT[i], CSI[j], ICDSQ[k], PROMIS[l] Global Health, bloating, constipation, diarrhea, cancer, stool change (Bristol stool chart) • GFD adherence/compliance (eg, histology, dietitian interview, adherence questionnaire, antitissue transglutaminase antibodies • Mortality • Quality of life: IGFDQ[m], WPAI:SHP[n] (Timing/follow-up: no minimum, except for RQs 3 and 5: ≥3 mo)	**RQs 1-6:** No results on outcomes of interest (Timing/Follow-up: none excluded, except for RQs 3 and 5: <3 mo)

(*continued on next page*)

Table 2. Celiac disease systematic review search plan (*continued*)

	Include	Exclude
Study designs	**RQ 1,4**: Randomized controlled trials, clinical controlled studies, observational studies (cohort, case control studies, cross-sectional) **RQs 2-3,5-6:** Randomized controlled trials, clinical controlled studies, observational studies (cohort, case control studies, cross-sectional)	**RQ 1,4:** Narrative reviews, case studies, case report, case series, noncomparative reviews, letters to the editor, systematic review, meta-analysis **RQs 2-3,5-6:** Narrative reviews, case studies, case report, case series, noncomparative reviews, letters to the editor, systematic review, meta-analysis
Size of study groups	**All RQs:** -Clinical controlled studies: N $\geq$10 for each study group -Observational studies: N $\geq$30	**All RQs:** -Clinical controlled studies: N $<$10 for each study group -Observational studies: N $<$30
Study drop out rate	**All RQs:** $\leq$30%	**All RQs:** $>$30%
Language	**All RQs:** English language	**All RQs:** Non-English language
Year range	**All RQs:** January 2007-present	**All RQs:** Before 2007

CDAT,; CDSD,; CSI,; ICDSQ,; IGFDQ,; , PROMIS,; WPAI:SHP
[a]RQ = research question.
[b]MNT = medical nutrition therapy.
[c]RDN = registered dietitian nutritionist.
[d]FODMAP = low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols diet.
[e]GFD = gluten-free diet.
[f]BMI = body mass index.
[g]DEXA = dual x-ray absorptiometry.
[h]CDSD = Celiac Disease Symptom Diar.
[i]CDAT = Celiac Dietary Adherence Test.
[j]CSI = Celiac Symptom Index.
[k]ICDSQ = Impact of Celiac Disease Symptom Questionnaire.
[l]PROMIS = Patient-Reported Outcomes Measurement Information System Global Health.
[m]IGFDQ = Impact of a Gluten-Free Diet Questionnaire.
[n]WPAI:SHP = Work Productivity and Activity Impairment Questionnaire: Specific Health Problem.

Table 3. Definitions for recommendation strength and grades for certainty of evidence for Academy of Nutrition and Dietetics evidence analysis center systematic review conclusion statements and recommendations

Strength of guideline recommendation	Implications for clinicians	Certainty of evidence from systematic review	Definition of grades for certainty of evidence
1 (Strong)	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are unlikely to be needed to help individuals make decisions consistent with their values and preferences	A: High	We are very confident that the true effect lies close to that of the estimate of the effect
		B: Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
2 (Weak)	Recognize that different choices will be appropriate for different people, and that you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may be useful in helping individuals making decisions consistent with their values and preferences. Clinicians should expect to spend more time with people when working toward a decision	C: Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
		D: Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect
Consensus	Recommendation is based on clinical expertise and experience with client values. Thus, different choices will be appropriate for different people, and you must help each patient arrive at a management decision consistent with patient values or preferences	Unclear or unavailable	Evidence from the systematic review was unavailable or unclear

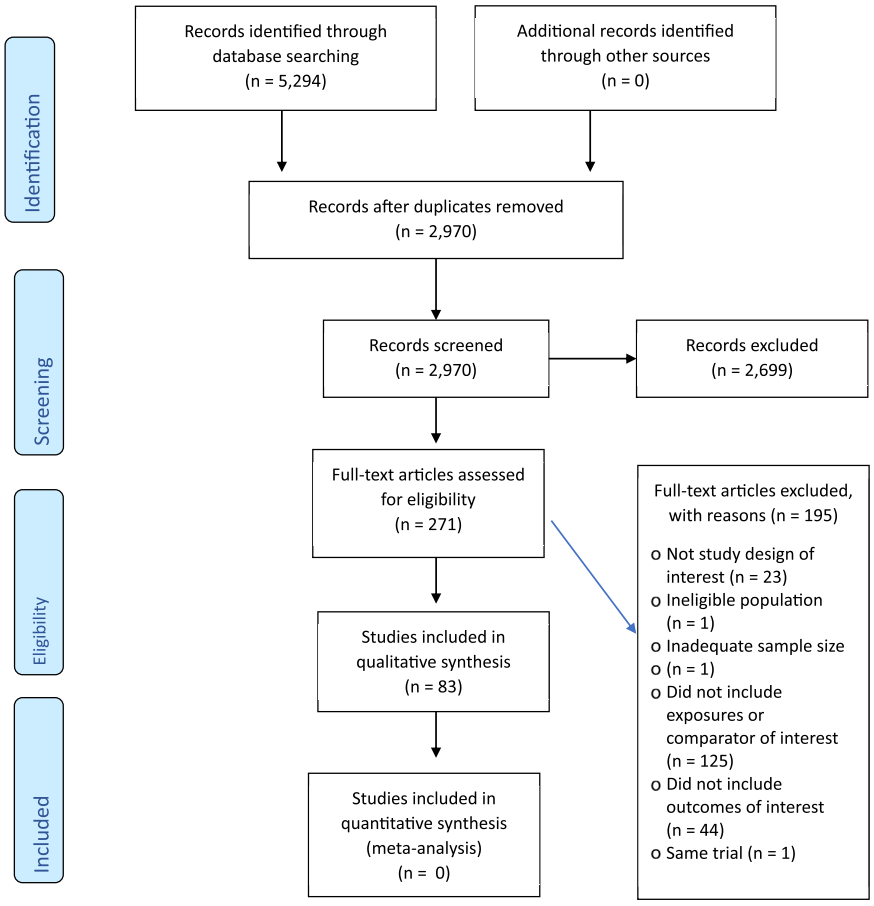


Figure. Search strategy flow diagram for literature examining the health effects of nutrition interventions on nutrition and health outcomes among those with celiac disease.