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Effectiveness of the low-FODMAP diet in improving non-celiac gluten sensitivity: a systematic review

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Abstract

Non-celiac gluten sensitivity is characterised by the presence of gastrointestinal and extraintestinal symptoms following gluten ingestion. Recent studies suggested an association between non-celiac gluten sensitivity and the consumption of fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP). This systematic review aimed to examine literature evidence on the relationship between non-celiac gluten sensitivity and FODMAP intake. A comprehensive search was carried out for randomised clinical trials addressing gastrointestinal symptoms as the primary outcome, published between 2010 and 2020 in Portuguese, English or Spanish, and indexed in Scopus, PubMed, SciELO, Cochrane Library, CINAHL, Embase or VHL (LILACS) databases. The systematic review was performed using the population, intervention, comparison and outcome (PICO) framework. A total of 1133 articles were retrieved for further assessment. Three articles were selected for systematic review, one of which included two interventions with different periods and assessments. Quality of evidence was assessed according to the GRADE protocol. The selected articles used different instruments to measure gastrointestinal symptoms and quality of life, hindering comparison of data. Clinical trials identified an association between decreased gastrointestinal symptoms and FODMAP restriction. There are few studies on the topic, and those available used different instruments to assess gastrointestinal symptoms and quality of life. Nevertheless, current evidence supports the gluten-free diet still represents first-line therapy. However, a FODMAP restriction can decrease gastrointestinal symptoms in individuals with non-celiac gluten sensitivity. Further research is needed to confirm this finding.

Key words: **Non-celiac gluten sensitivity: FODMAP: Gastrointestinal symptoms: Gluten: Quality of life**

Gluten is a generic term applied to the storage proteins found in wheat, barley and rye. Gluten contains large amounts of gliadin, which is resistant to degradation by gastric acids, pancreatic enzymes and the brush border enzymes, hindering digestion[1].

Some individuals develop a reaction to gluten, showing symptoms after consuming this protein. One of the diseases related to gluten consumption is non-celiac gluten sensitivity (NCGS). The diagnosis of this little-studied condition is exclusively clinical, identified by exclusion of other gluten-related disorders, as celiac disease, wheat allergy and gluten ataxia, and improvement in symptoms after exclusion of gluten from the diet, given that, to date, no specific biochemical or immunological markers have been discovered[2]. Manifestations of NCGS include gastrointestinal symptoms, such as abdominal pain, constipation, indigestion, diarrhoea and flatulence, as well as extra-intestinal symptoms, such as migraine, mental confusion, fatigue, depression, anxiety and body aches[3]. According to the literature, when individuals diagnosed with NCGS are placed on a gluten-free diet, they show improvement in symptoms[4,5]. NCGS affects mainly adult women and appears to be more prevalent than other gluten-related disorders. The first cases were reported about 30 years ago; however, only recently have the disease and its mechanism of action gained interest in the scientific community, after numerous reports of improvement in symptoms with the exclusion of gluten from the diet[6].

Fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) are naturally present or added to foods. These carbohydrates undergo fermentation by intestinal bacteria and cause changes in water absorption. FODMAP pass through the small intestine without being digested and reach the intestinal colon where they are fermented by microbiota, producing SCFA. These metabolites provide several benefits to healthy individuals, including protection of the colon epithelium and immune system, participation in appetite regulation and

Abbreviations: FODMAP, Fermentable oligosaccharides, disaccharides, monosaccharides and polyol; NCGS, non-celiac gluten sensitivity; PICO, population, intervention, comparison, outcome; VAS, visual analogue scale.

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beneficial alteration of lipid metabolism[7]. However, in addition to SCFA, fermentation of FODMAP leads to methane and hydrogen production, causing bloating and flatulence in some individuals[8].

The presence of FODMAP in the intestinal lumen alters osmolarity, as the amount of solute becomes greater than that within enterocytes. Such a change increases the amount of water in the lumen, which, in healthy individuals, improves intestinal transit and stool consistency. In more sensitive individuals, however, this condition can cause diarrhoea or bloating[9]. Thus, low FODMAP diets have been proposed as dietary treatment for diseases that cause intestinal hypersensitivity, such as irritable bowel syndrome[10], to reduce symptom severity and improve the quality of life of patients.

Recently, researchers have investigated the effects of FODMAP on the occurrence of NCGS manifestations[11]. FODMAP, especially fructans, are present in foods that also contain gluten, such as bread, pasta and breakfast cereals[12]. Although NCGS can be triggered by the consumption of gluten-containing foods, its aetiology is not yet well elucidated. There is still no consensus on the main cause of NCGS symptoms[13]. This review aimed to examine scientific literature on the relationship between FODMAP intake and NCGS symptoms.

Methods

This systematic review followed the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) and was registered in the PROSPERO database (CRD42020199164). Article selection was based on the PICO (population, intervention, comparison, outcome) framework, as follows:

P: adults of both sexes aged 18–60 years and diagnosed with NCGS;
I: FODMAP-restricted diet;
C: unrestricted diet, rich in FODMAP and
O: improvement of gastrointestinal and extraintestinal signs and symptoms as well as quality of life.

Study eligibility criteria

The following eligibility criteria were used: randomised clinical trials, published between 2010 and 2020 in Portuguese, English or Spanish, without geographical restriction. Exclusion criteria included studies with pregnant women or individuals with celiac disease, wheat allergy, gluten ataxia, dermatitis herpetiformis, irritable bowel syndrome, short bowel syndrome, Crohn's disease, ulcerative colitis or inflammatory bowel disease.

Search strategy

For the systematic search of the literature, uniterms were defined according to the objectives of this review using Medical Subject Headings of the USA the National Library of Medicine (MeSH), Health Sciences Descriptors (DeCS) and keywords of articles identified in a previous search. The search was conducted in Scopus, PubMed, SciELO, Cochrane Library, CINAHL, Embase and VHL (LILACS) databases in April 2020 by the three authors.

Uniterms were separated into two groups, the first related to diagnosis (NCGS) and the second to treatment (FODMAP). Uniterms in the same group were separated by the Boolean operator 'OR', whereas groups were separated by the Boolean operator 'AND'. The simplified search strategy was as follows ("Non-celiac gluten sensitivity" OR "Gluten sensitivity" OR "Gluten sensitive" OR "Gluten-related disorders" OR "Gluten intolerance" OR "Spectrum of gluten-related disorders" OR "Sensibilidad no celiaca al gluten" OR "Non-celiac wheat sensitivity OR "non-celiac") AND ("Low fodmap diet" OR "FODMAPs" OR "FODMAP" OR "Fermentable oligo-, di- and monosaccharides and polyols" OR "monossacarídeos" OR "monosaccharides" OR "monosacáridos" OR "dissacarídeos" OR "disaccharides" OR "disacáridos" OR "oligossacarídeos" OR "oligosaccharides" OR "oligosacáridos" OR "polioles" OR "polióis" OR "polyols" OR "frutossacarídeos" OR "fructooligosaccharides" OR "fructooligosacáridos" OR "frutose" OR "fructose" OR "fructosa"). The search strategy used in each platform can be found in Table S1 (online Supplementary material). To ensure that all relevant studies were selected, each author conducted a separate search.

Article selection

The selection of eligible articles was carried out independently and in pairs, by two researchers (RAK and LBAFD), using RAYYAN software[14]. The first selection was made by reading the titles. Then, the abstract of the chosen articles was read, and articles were further selected considering the PICO framework. At both stages, any discrepancies were resolved by a third researcher (ABN). Following this stage, the remaining articles were read in full and the data extracted.

Data extraction

As a strategy to control measurement bias, data extraction was performed independently by two researchers (LBAFD and RAK). Extracted data included authorship, year, location, intervention, follow-up time, variables, outcome and conclusion. Variables were extracted from articles but are not reported in the extraction table. Any discrepancies were resolved by a third researcher (ABN). The risk of bias was evaluated using the Cochrane tool (Risk of Bias 2·0), specific for randomised trials.

Results

Literature search

Initially, 1133 articles were retrieved, 203 of which were duplicates, including identical articles published in different languages. After duplicate exclusion, the titles of the remaining 930 articles were read, and 842 articles were excluded on the basis of the following criteria: studies on different topics, systematic reviews, editorials, letters and interventions with children and/or adolescents. In the subsequent stage of selection, the abstracts of the remaining eighty-eight articles were read. Of these, ten articles were selected for full reading, seven of which were excluded because they were unfinished manuscripts (only the abstracts were published). Finally, three articles that met all inclusion criteria were included in this review. The selected papers are original articles published between 2013

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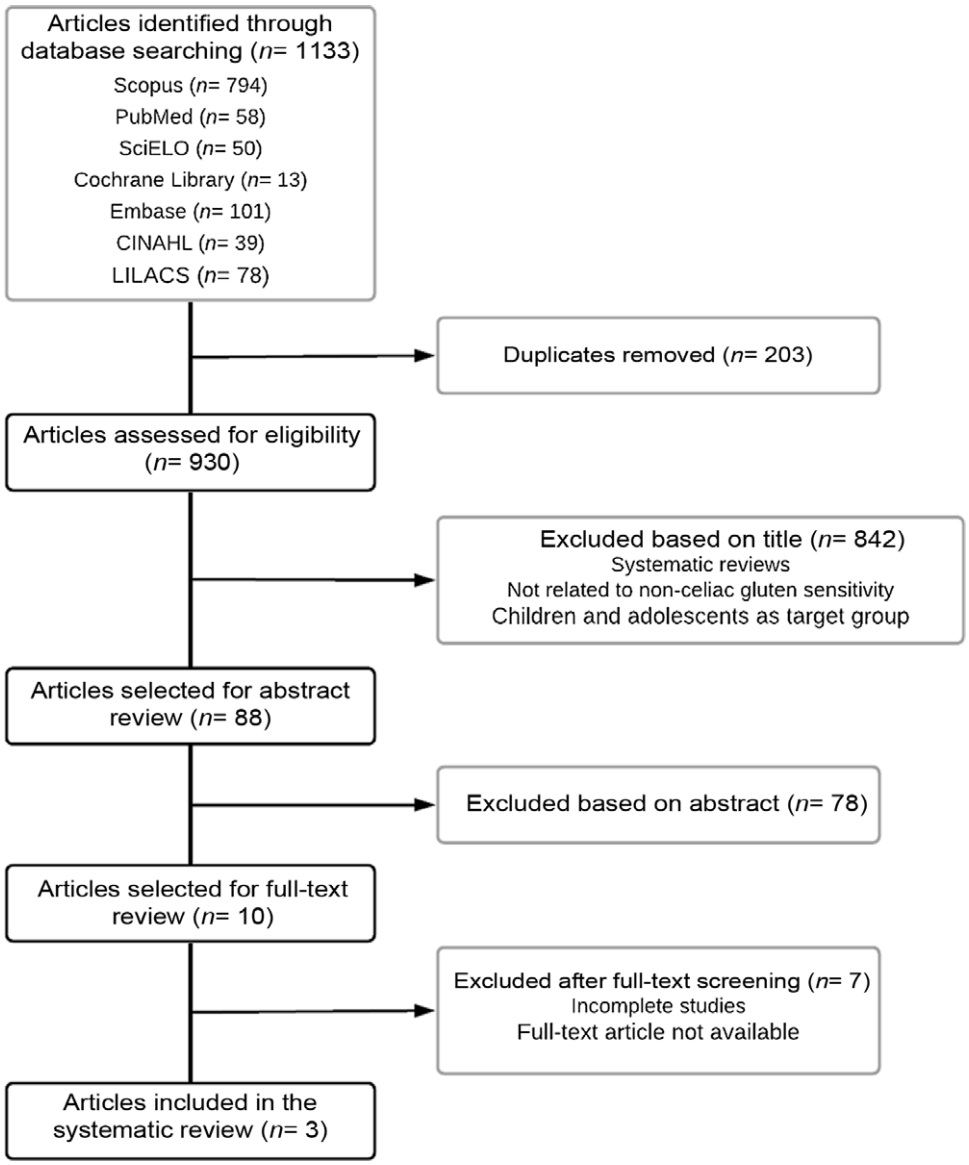

Fig. 1. Flowchart of the study selection process.

and 2018 on low-FODMAP dietary interventions in adult individuals with NCGS. Fig. 1 shows a flowchart of the article selection process.

Study sample and instruments

The selected studies were randomised clinical trials conducted in Germany, Australia or Norway. In total, 125 individuals were analysed, 115 of which were self-diagnosed with NCGS and 10 formed the control group; 106 participants were women and 19 men and the mean age was 42·5 years. In all studies, diagnosis of celiac disease was excluded by examinations performed at baseline. The study by Biesiekiesrki *et al.*[15] comprised two distinct interventions; thus, for this review, the article will be treated as two distinct studies. The selected articles analysed several variables; however, only those that were within the scope of the review (outcome of gastrointestinal symptoms and quality of life) were assessed.

The studies used different instruments to evaluate outcomes related to gastrointestinal symptoms, lacking standardisation. Biesiekiesrki *et al.*[15] used a visual analogue scale (VAS), Dieterich *et al.*[16] used the Gastrointestinal Symptom Rating Scale for Irritable Bowel Syndrome, and Skodje *et al.*[17] used both. VAS is used for measuring symptom intensity: a 10-cm horizontal line is anchored by the numbers 0 (no pain) and 10 (unbearable pain), and results are scaled by measuring the distance in millimetres. The Gastrointestinal Symptom Rating Scale for Irritable Bowel Syndrome is a 13-item questionnaire with scores ranging from 1 to 7, where 7 represents more severe symptoms. Instruments used to assess quality of life and psychological symptoms also differed between studies. Biesiekierski *et al.*[15] applied the Daily Fatigue Impact Scale and the Short

Form-36 (SF-36), Skodje *et al.*[17] used the Giessen Subjective Complaints List and the VAS to assess quality of life specific to symptoms, and Dieterich *et al.*[16] used the Psychological General Well-Being Index (PGWBI). The SF-36 is a scale in which the higher the result, the better the quality of life, whereas Daily Fatigue Impact Scale and TGSC analyse the severity of outcomes.

Study quality and risk of bias

The GRADE approach revealed some concerns about the risk of bias of studies by Dieterich *et al.*[16] and Skodje *et al.*[17] Both interventions of the study of Biesiekierski *et al.*[15] were classified as having a low risk of bias. Biases were mainly observed in the measurement of outcomes, selection of reported results and deviations from the intended intervention. The study of Dieterich *et al.*[16] was not a double-blind clinical trial because, according to the authors, participants would easily be able to identify which diet they had been assigned to by consulting the internet. In this case, participants' knowledge of their treatment group might have interfered with the outcome. Skodje *et al.*[17] did not report the results of gastrointestinal symptoms assessed by the VAS scale; results were stratified by intervention period only. Graphical representations of the risk of bias for each study and analysis of the domains are presented in Fig. 2.

Data extraction and analysis

Table 1 provides a summary of the characteristics, results and conclusions of the selected articles.

Gastrointestinal symptoms

The studies used different instruments and protocols for evaluation of variables of interest. By using VAS, Biesiekierski *et al.*[15] (both interventions) and Skodje *et al.*[17] found that FODMAP and, more specifically, fructans may cause gastrointestinal symptoms in NCGS patients. Biesiekierski *et al.*[15] reported improvements in abdominal pain, bloating, fatigue, flatulence and stool consistency ($P < 0{\cdot}0001$) with dietary restriction of FODMAP. Both studies identified that bloating improved with the exclusion and worsened with the inclusion of FODMAP[15,17].

Using Gastrointestinal Symptom Rating Scale for Irritable Bowel Syndrome, Dieterich *et al.*[16] and Skodje *et al.*[17] associated low-FODMAP diets with less severe gastrointestinal

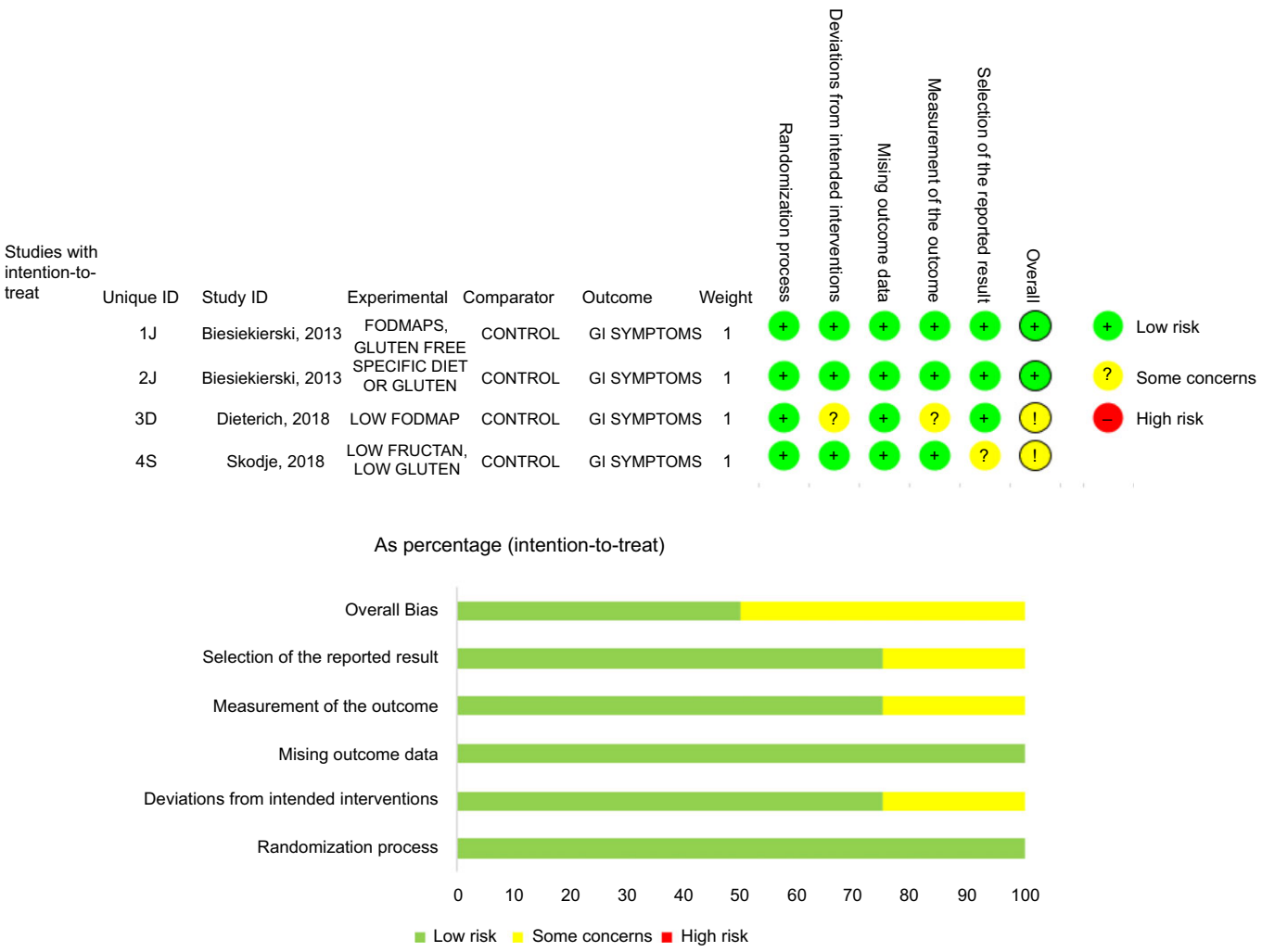

Fig. 2. Risk of bias of selected studies, as assessed using the Cochrane Collaboration's tool.

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Table 1. Data extraction and analysis

Reference, country	Type of study	Sample size	Sample characteristics	Methods	Outcomes		
					Gastrointestinal symptoms	Quality of life	Conclusions
Biesiekierski *et al.* (2013)[15], Australia Intervention 1	Randomised, double-blind, crossover, placebo-controlled, clinical trial	*n* 37	Mean age: 45 years 31 women (84 %) and 6 men (16 %)	Treatments: - Low-fermentable oligosaccharides, disaccharides, monosaccharides and polyol (FODMAP) diet - High-gluten diet (16 g gluten/d) - Low-gluten diet (2 g gluten/d + 14 g whey protein/d) - Control diet (16 g whey protein/d) Intervention (10 weeks): - 1 week of baseline (gluten-free diet low in FODMAP) - 2 weeks of FODMAP restriction - 1 week for each dietary treatment - at least 2 weeks of washout between diets Assessment scales: - Gastrointestinal symptoms scored on a VAS. - Fatigue levels were assessed using the D-FIS, an unstructured hedonic scale.	Visual analogue scale (VAS) - There was a significant reduction in gastrointestinal symptoms in the reduced FODMAP group compared with baseline ($P < 0{\cdot}0001$); differences were significant for abdominal pain, constipation and tiredness but not for nausea ($P = 0{\cdot}149$). - Only 6 participants (16 % of sample) had an increase in overall abdominal symptoms (>20 mm) when placed on the high gluten diet compared with the low-FODMAP diet. - Seven participants (19 % of total cohort) had symptomatic responses to whey.	Daily fatigue impact scale (D-FIS) - The low-FODMAP diet was associated with a low D-FIS score ($1{\cdot}95 \pm 0{\cdot}53$) compared with baseline ($5{\cdot}04 \pm 0{\cdot}87$, $P = 0{\cdot}0006$). - High-gluten ($P = 0{\cdot}005$), low-gluten ($P = 0{\cdot}004$) and control ($P = 0{\cdot}003$) diets resulted in increased fatigue compared with the reduced FODMAP diet. - Bloating and tiredness symptoms worsened with the low-gluten and control diets.	- Gastrointestinal symptoms and fatigue improved with reduced FODMAP intake compared with baseline. - The control group experienced gastrointestinal symptoms, suggesting a possible nocebo effect triggered by stress during the intervention. - The authors argued that gluten might only induce symptoms when combined with a moderate intake of FODMAP. Further studies are needed to confirm this hypothesis. - Participants showed a significant improvement in gastrointestinal symptoms during all interventions.
Biesiekierski *et al.* (2013)[15], Australia Intervention 2	Randomised, double-blind, crossover, placebo-controlled, clinical trial	*n* 22	Mean age: 48 years 17 women (77 %) and 5 men (23 %)	Treatments: - A baseline period consisting of a gluten-free, dairy-free, low-FODMAP diet without food additives (background diet) - 16 g/d whey protein isolate - 16 g/d gluten - placebo (no additional protein) Intervention (18 d): - 3 d of baseline - 3 d for each dietary treatment - 3 d of washout between diets	VAS - There were no differences in overall symptoms between baseline and the third day of each dietary treatment. - Changes in individual symptoms were similar between the three diets ($P > 0{\cdot}209$)	D-FIS - There were no differences in symptoms related to quality of life between gluten ($2{\cdot}05 \pm 1{\cdot}44$), whey ($1{\cdot}85 \pm 1{\cdot}03$), and placebo ($2{\cdot}42 \pm 1{\cdot}45$) diets. - No comparisons were made between the three diets and the reduced FODMAP period.	- The dairy-free, additive-free diet was implemented to avoid potential triggers of gastrointestinal symptoms. - There were no significant changes in gastrointestinal and psychological symptoms between the three diets, possibly because the dose of gluten (16 g/d) was not sufficiently high to trigger these responses.

Table 1. (*Continued*)

Reference, country	Type of study	Sample size	Sample characteristics	Methods	Outcomes		Conclusions
					Gastrointestinal symptoms	Quality of life	
				Assessment scales: - Gastrointestinal symptoms scored using VAS. - Fatigue levels were assessed using the D-FIS.			
Skodje *et al.* (2018)[17], Norway	Randomised, double-blind, crossover, placebo-controlled, clinical trial	*n* 59	Mean age: 43·7 years 53 women (90 %) and 6 men (10 %)	Challenges: - Muesli bar containing 2·1 g fructan - Muesli bar containing 5·7 g gluten - Gluten-free, low-FODMAP muesli bar Intervention (6 weeks): - 1 week of baseline (gluten-free diet) - 1 week for each dietary challenge - 1 week of washout between treatments Assessment scales: Gastrointestinal symptoms were assessed using the Gastrointestinal Symptom Rating Scale for Irritable Bowel Syndrome (GSRS-IBS) and VAS. Quality of life and fatigue were measured using the Short Form-36 (SF-36) questionnaire, VAS and the Giessen Subjective Complaints List (GSCL).	VAS - During the first week of dietary treatment (period 1), there was a significant difference in VAS scores across gluten, placebo and fructan challenges ($P = 0{\cdot}04$), but pairwise comparisons were NS ($0{\cdot}52 \leq p \leq 1{\cdot}00$). - In period 2, the difference across challenges was significant ($P < 0{\cdot}008$). Symptoms were significantly worse on days 3, 6 and 7 in the fructan challenge group than in the placebo group ($P < 0{\cdot}006$). - In period 3, there was a significant interaction between day of intervention and dietary challenge ($p_{interaction} = 0{\cdot}02$) as well as a significant interaction effect of challenge, period and day on bloating symptoms ($p_{interaction} = 0{\cdot}02$). - In period 3, bloating scores were higher after the fructan challenge. GSRS-IBS Overall symptoms: There was a significant difference in overall symptom scores across the three challenges ($P = 0{\cdot}04$). The fructan challenge promoted an increase ($P = 0{\cdot}049$) in overall gastrointestinal symptoms compared with the gluten challenge. Compared with the placebo, fructan ($P = 0{\cdot}19$) and gluten ($P = 0{\cdot}99$) bars produced no significant increase in overall symptoms. Mean GSRS-IBS scores were higher after the fructan challenge in the three periods ($P = 0{\cdot}03$), with a	SF-36 Vitality: There was a significant difference in vitality scores across the three challenges ($P = 0{\cdot}04$), with the fructan group having the lowest mean score (38·6). Participants in gluten and placebo groups had mean vitality scores of 44·7 and 44·0, respectively. VAS Weakness: The gluten challenge resulted in the lowest weakness scores (32·4), differing significantly from the other groups ($P = 0{\cdot}02$). GSCL Weakness: Compared with the gluten challenge, the fructan challenge significantly increased ($P = 0{\cdot}02$) weakness. Mean values for gluten, placebo and fructan groups were 32·8, 33·5, and 42·5, respectively. Vitality: Compared with the gluten challenge, the fructan intervention resulted in a significant decrease in vitality ($P = 0{\cdot}04$).	- According to VAS scores, overall symptoms were significantly worse after the fructan challenge in period 2; in period 3, this difference was NS. - GSRS-IBS scores showed that symptoms were worse after the fructan challenge than the gluten challenge, but values were not significantly different from the placebo. - Only bloating increased significantly after the fructan challenge compared with the gluten challenge. - Fructans are more likely to induce symptoms in people with non-celiac gluten sensitivity, affecting mainly the quality-of-life dimensions vitality and weakness.

Table 1. (*Continued*)

Reference, country	Type of study	Sample size	Sample characteristics	Methods	Outcomes		Conclusions
					Gastrointestinal symptoms	Quality of life	
					significant difference between fructan and placebo challenges in the second period ($P = 0{\cdot}03$). Bloating: There was a significant difference in mean bloating scores across the three challenges ($P = 0{\cdot}004$). Compared with the gluten group, the fructan challenge significantly increased bloating ($P = 0{\cdot}003$). Gluten ($P = 0{\cdot}84$) and fructan ($P = 0{\cdot}07$) bars did not worsen bloating symptoms compared with the placebo. Diarrhoea, pain and satiety: Diarrhoea, pain and satiety scores were higher after the fructan challenge, but differences were NS ($0{\cdot}07 \leq p \leq 0{\cdot}15$).		
Dieterich *et al.* (2019)[16], Germany	Randomised, placebo-controlled, clinical trial	*n* 29	Mean age: 33·3 years 22 women (76 %) and 7 men (24 %)	Treatments: - Gluten diet (10 g/d gluten) - Low-FODMAP diet - Gluten-free diet Intervention (8 weeks and 5 d) - 4 weeks of baseline (10 g/d gluten) - 2 weeks of low-FODMAP diet - 5 d of washout - 2 weeks of gluten-free diet Assessment scales: Psychological General Well-Being Index (PGWBI) and GSRS	GSRS - At baseline, gastrointestinal symptoms were significantly different between non-celiac gluten sensitivity (NCGS) patients and the control ($13{\cdot}8 \pm 6{\cdot}2$ *v.* $3{\cdot}5 \pm 2{\cdot}4$, $P < 0{\cdot}001$) - After the low-FODMAP diet treatment, the symptoms of the NCGS group improved significantly ($8{\cdot}7 \pm 5{\cdot}2$, $P = 0{\cdot}001$), mainly reflux, abdominal pain and indigestion. Symptoms also improved when participants were on a gluten-free diet ($P > 0{\cdot}05$). - The control group showed improvements in abdominal pain ($P = 0{\cdot}045$) and in the symptom complex ($P = 0{\cdot}031$) under all treatments. - In the NCGS group, diarrhoea and abdominal pain had a more pronounced improvement with the gluten-free diet than with the low-FODMAP diet ($P = 0{\cdot}032$, $P = 0{\cdot}001$). This was also observed for symptoms in general ($P = 0{\cdot}004$).	PGWBI - Psychological parameters at baseline showed that patients with NCGS had a significantly compromised psychological well-being compared with the control ($P < 0{\cdot}01$). - With the low-FODMAP diet, there was an improvement in psychological symptoms in the NCGS group ($74{\cdot}2 \pm 18$, $P = 0{\cdot}001$) and even more so with the gluten-free diet, as compared to the control ($84{\cdot}5 \pm 17{\cdot}3$).	- The low FODMAP diet improved reflux, abdominal pain and indigestion. However, the gluten-free diet showed better results. - The low-FODMAP diet led to improvements in psychological symptoms. - Psychological parameters improved with any of the diets compared with baseline.

symptoms, particularly in relation to abdominal pain. For other gastrointestinal symptoms, such as reflux, indigestion and diarrhoea, fructan consumption was associated with symptom worsening. In these studies, gluten-free diets were compared with low-FODMAP diets, the gluten-free diet produced superior improvements in gastrointestinal symptoms, including bloating, diarrhoea and abdominal pain.

One of the factors limiting study comparison, in addition to differences in assessment scales, was the difference between dietary interventions. Biesiekierski *et al.*[15] and Dieterich *et al.*[16] used low-FODMAP diets, whereas Skodje *et al.*[17] used muesli bars containing fructans (a type of FODMAP). Furthermore, in the first intervention of Biesiekierski *et al.*[15], it was not possible to compare between gluten-free, gluten-containing, low-FODMAP and placebo diets. Overall, the clinical trials revealed an association between increased gastrointestinal symptoms and FODMAP consumption in patients with NCGS.

Quality of life

The three studies measured psychological symptoms and quality of life by using different instruments and scales, making it difficult to compare them. In general, studies were unanimous in identifying that dietary intake of FODMAP worsened psychological symptoms at baseline. Low-FODMAP diets were associated with fewer psychological symptoms in Dieterich *et al.*[16] and Biesiekierski *et al.*[15] compared with the gluten-free diet. These findings can be attributed to the severity of symptoms reported by participants, which directly affect quality of life. Such results were corroborated by those of Skodje *et al.*[17], who found that the fructan diet worsened weakness and vitality in comparison with the gluten diet and enhanced the intensity of symptoms related to quality of life.

Discussion

The low-FODMAP diet is not yet well established. A protocol was developed in 1999 by Gibson and Shepard at the Monash University, Melbourne, and proposed, in 2005, for individuals with Crohn's disease and, posteriorly, irritable bowel syndrome by the same researchers. However, the diet is based on the typical foods and food culture of Australia, not providing knowledge on the amount of FODMAP in the diets of other populations. The study of Biesiekierski *et al.*[15] was developed in Australia, and those of Dieterich *et al.*[16] and Skodje *et al.*[17] were conducted in Europe; all were likely influenced by local food cultures. None of the studies specified the foods that composed the low-FODMAP diets.

Skodje *et al.*[17] did not use a low-FODMAP diet; rather, the FODMAP treatment consisted of food bars containing fructans. Fructan is but one of the existing FODMAP, generating the possibility that other factors interfered with symptoms, given that diet was not controlled. In the study of Biesiekierski *et al.*[15], the entire diet was supplied to patients. In the other studies, researchers provided dietary guidelines to participants for adherence to a low-FODMAP diet, thereby generating the possibility of bias, as other factors possibly influencing the onset of symptoms could not be controlled. Furthermore, this method makes it difficult to monitor adherence to diets.

According to Muir *et al.*[9], the cut-off values for foods to be considered rich in FODMAP are the following: <0·15 g of fructose per serving; <0·3 g of oligosaccharides per serving in grain and cereal products; <0·2 g of oligosaccharides per serving in fruits, vegetables and all other products or <0·2 g of sorbitol/mannitol per serving. These values refer to a clinical trial with patients with irritable bowel syndrome; thus, the tolerable amount of these substances for individuals with NCGS has not yet been described. Furthermore, there may be individual variability in the tolerance to FODMAP, as well as specific foods that may increase sensitivity, although there have been no reports of such occurrence in current studies on FODMAP[18].

Foods that contain gluten are included in the list of foods that contain FODMAP, because wheat contains a huge number of oligosaccharides, e.g. fructans. This fact could justify why a gluten-free diet (or a wheat-free diet) improves gastrointestinal symptoms in individuals with NCGS, as it simultaneously removes foods rich in FODMAP and fibres, thereby reducing intestinal bacterial fermentation. In the evaluated studies, the gluten-free diet led to greater improvement in individual gastrointestinal symptoms than the low-FODMAP diet, demonstrating that gluten seems to have a greater influence on individuals with NCGS than FODMAP. It should be noted that low-FODMAP diets may generate psychosocial problems, resulting from the high restriction of food items, hindering socialisation and causing changes to the intestinal microbiota resulting from reduced fibre intake[19].

One of the limitations of this review was the low number of studies on the topic; this is attributed to the fact that both topics have been studied for a short time. Furthermore, it was not possible to perform a meta-analysis of the review given the scarcity of data and the use of scales that cannot be compared. The four studies used different intervention periods and segments, hindering conclusive results regarding symptom improvement with low-FODMAP diets. Further studies are needed to analyse the effect of low-FODMAP diets in improving gastrointestinal symptoms and quality of life in individuals with NCGS and to standardise instruments used for outcome evaluation between interventions.

Conclusion

Analysis of the selected studies revealed that FODMAP can increase gastrointestinal symptoms in patients with NCGS and worsen quality of life and psychological symptoms. However, improvements in gastrointestinal symptoms were observed when these individuals adhered to gluten-free diets, without the need for FODMAP restriction. More studies are needed with scales and methods that can be compared with obtain resolutions with greater clinical applications for the study population.

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There are no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114522002884

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