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Probiotic Use in Celiac Disease: Results from a National Survey

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ABSTRACT

Background & Aims: Patients with celiac disease (CD) commonly use supplements for perceived health benefits despite scant evidence. We aimed to characterize the prevalence and predictors of probiotic use among CD patients.

Methods: We analyzed data from iCureCeliac®; a patient-powered research network questionnaire distributed by the Celiac Disease Foundation. We included adults with self-reported CD who answered questions regarding demographics, diagnosis, symptoms, and treatment. We compared probiotic users versus probiotic non-users and subsequently performed multivariable logistic regression, assessing for independent predictors of probiotic use.

Results: 4,909 patients met the criteria for inclusion in the study. Of these, 1,160 (23.6%) responded to a question regarding probiotic use. The mean age of participants was 38.8 years and 82% were female. 381 patients (33%) reported using probiotics. More probiotic users sought nutritional counseling at time of diagnosis (36% vs. 30%, p=0.05) and remained symptomatic despite a gluten-free diet (40% vs. 25%, p <0.001). Probiotic users had worse scores on the pain subscale of the SF36 (63.7±21.6 vs. 69.5±22.1, p=0.006). On multivariable analysis, patients diagnosed after age 50 (OR=2.04, 95%CI: 1.37-3.04), and those with persistent symptoms despite a gluten-free diet (OR=1.94, 95%CI: 1.44-2.63) were more likely to use probiotics.

Discussion: In this large study of a national CD registry, roughly one-third of CD patients reported using probiotics. Patients diagnosed later in life were more likely to use probiotics and those who remained symptomatic despite a gluten-free diet were twice as likely to take probiotics. Patients may be seeking additional means of treatment for persistent symptoms.

Key words: celiac disease – probiotics – gluten free diet – biopsy – dietary supplement.

Abbreviations: CD: celiac disease; CDQOL: Celiac Disease Quality of Life; GFD: gluten-free diet; PPRN: patient-powered research network; SF: short form.

INTRODUCTION

Celiac disease (CD) is an immune-mediated enteropathy triggered by gluten ingestion in genetically susceptible individuals [1]. Celiac disease affects 0.7-1% of Americans, making it one of the most common inflammatory conditions of the digestive system in the United States [2, 3]. The primary treatment for CD is complete abstinence from dietary products containing gluten. Yet, maintaining a strict gluten-free diet (GFD) is challenging for many individuals, and at least a quarter of adult CD patients report persistent symptoms despite strict adherence [4, 5]. At present, there is limited evidence for additional therapeutic options [6]. However, there has been increasing interest among patients with CD to take dietary supplements for perceived health benefits [7].

Probiotics have gained significant popularity among patients with CD and in the general population [7, 8]. Probiotics are live, ingestible microorganisms that can alter the gastrointestinal microbiome and may confer health benefits onto their host [9]. Despite the many studies examining their use, there is scant high-quality evidence supporting the use of probiotics in gastrointestinal disease. Guidelines issued by the American Gastroenterological Association (AGA) give conditional recommendations for the use of probiotics for

the prevention of *Clostridium difficile* infection, pouchitis in surgically resected inflammatory bowel disease patients, and necrotizing enterocolitis, though the quality of supporting evidence remains limited [8].

Celiac disease and other autoimmune disorders of the gut are associated with abnormal composition and function of the intestinal microbiome [10]. It has been hypothesized that probiotic supplementation may have an impact on CD pathophysiology via three potential mechanisms: (1) digestion of gluten proteins, (2) maintenance of the intestinal barrier by preventing access of immunogenic polypeptides to lamina propria and (3) restoration of gut microbial homeostasis and regulation of the innate and adaptive immune systems [11]. There is currently a paucity of evidence supporting the use of probiotics to improve histopathologic or clinical manifestations of CD. Nevertheless, probiotics are among the most frequently used supplements in patients with CD for unclear reasons [7].

The aim of this study was to characterize the prevalence and predictors of probiotic use among CD patients using data from iCureCeliacTM, a voluntary, patient-powered research network questionnaire distributed by the Celiac Disease Foundation.

METHODS

Study Design

We performed a cross-sectional analysis utilizing questionnaire data from iCureCeliac® a voluntary, patient-powered research network (PPRN). Beginning in January 2016, the questionnaire was distributed to patients via the Celiac Disease Foundation website. Patients had the option to enter as much or as little data as they desired on an entirely voluntary basis with no financial incentive offered. Informed consent was obtained from each patient prior to completion of the survey. We included patients 18 years or older who indicated a diagnosis of CD in the questionnaire and who answered questions regarding probiotic use, symptoms, the method of diagnosis, and adherence to treatment that applied to our study question between the inception of the PPRN on January 30, 2016 and February 21, 2019. This study was approved by the Institutional Review Board of Columbia University Medical Center on July 21st, 2017.

Data Collection

We collected basic demographic information including age, gender, age at diagnosis, country of origin, and region within the United States. Data regarding patients' diagnosis were also extracted from the survey including means of diagnosis, whether the diagnosis was made by a physician or non-physician health care practitioner, where patients obtained their primary information about celiac disease, whether patients sought nutritional counseling at time of diagnosis, the Short Form (SF) 36 questionnaire, and the Celiac Disease Quality of Life (CDQOL) score. We also examined information about self-rated health on a 5-point scale, GFD adherence, and persistent symptoms despite adherence to a GFD.

Celiac Disease Quality of Life Score

The CD-QOL score, was previously developed by Dorn et al. [12] through focus groups, expert review, and pilot testing. It was shown to have high internal consistency and reliability. The final score contains 20 items in four domains (limitations, dysphoria, health concerns, inadequate treatment) with higher scores corresponding to better health states.

SF-36

The SF-36, first described by Ware and Sherbourne [13], is a 36-question survey incorporating 8 domains: limitations in physical activities due to health problems, limitations in social activities due to physical or emotional problems; limitations in activities due to physical health problems; physical pain; general mental health; limitations in usual role activities due to emotional health; energy, and general health perceptions. Questions are scored and scaled (either positively or negatively) so that higher scores correspond to better health states.

Statistical Analysis

We defined probiotic users as individuals who responded "Yes" to the following question: "Do you take a probiotic regularly (at least 3 times a week)." We compared probiotic users to probiotic non-users with regard to the above-listed variables using Chi-square tests for categorical values and Student's t-tests or Mann-Whitney U test (for non-parametric data) for continuous variables. We then analyzed data via multiple logistic regression, reporting adjusted odds ratios and 95% confidence intervals (CIs) to identify variables that were independently associated with probiotic use. After identifying significant differences on univariate analyses, we adjusted for the following variables in our multivariable analysis: age at diagnosis, gender, region, country, whether they sought nutritional counseling, primary information source, whether they keep to a strict GFD, whether they are still symptomatic, and how they were (serology, by biopsy, or by other test). We performed multiple logistic regression analysis both with and without significant SF-36 items to preserve power, as there were a limited number of respondents who answered all of the SF-36 questions. We used Stata version 16.0 (College Station, Tx) for all calculations and statistical analysis.

RESULTS

We identified 4,909 patients that met criteria for inclusion in the study. Of these, 1,160 (23.6%) patients responded to a question regarding probiotic use. The characteristics of our study population are shown in Table I. The subjects were predominantly female (82%). The mean age was 38.8 years (SD±17.4); 3,879 (79%) were diagnosed with CD based on intestinal biopsy, serologies or both. The mean age at diagnosis was 32.2 (SD±6.4) years; 85% of respondents were from the United States and the most common region of respondents 24.2% was in the Midwest; 38.6% of patients sought nutritional counseling at the time of diagnosis and 27.9% of patients use social media or an internet web page to obtain their primary information regarding celiac disease; 85% and 10.8% of respondents reported adhering to a strict GFD always or often, respectively. Notably, 50.4% of respondents reported ongoing symptoms, despite adherence to a GFD, although further detail on the nature of these symptoms was not included in the survey. Of the patients that responded to the question

regarding probiotic use (n = 1,160), 381 (32.8%) reported using probiotics to "aid in the digestion of gluten."

Table I. Baseline Characteristics

Gender (n=4,832)	
Female	3,958 (81.9)
Male	852 (17.6)
Other	22 (0.5)
Age (mean ± SD, n = 4,832)	**38.8 ±17.4**
<20	671 (13.9)
20-29	942 (19.5)
30-39	1,004 (20.8)
40-49	863 (17.9)
50-59	740 (15.3)
≥60	612 (12.7)
Age at diagnosis (mean±SD, n=1,613)	**32.2 ± 16.4**
<10 years old	167 (10.4)
10-29 years old	200 (12.4)
20-29 years old	366 (22.7)
30-39 years old	353 (21.9)
40-49 years old	265 (16.4)
≥50 years old	252 (16.2)
Country of origin (n=4,755)	
United States	4,172 (85.0)
Other	737 (15.0)
Region US (n= 4,056)	
Northeast	1,043 (21.3)
South	896 (18.3)
Midwest	1,190 (24.2)
West	922 (18.8)
Territories	5 (0.1)
Unknown/Outside US	853 (17.4)
Method of diagnosis (n=4,909)	
Biopsy of the intestine or small bowel during upper endoscopy	3,081 (62.8)
Serology	3,351 (68.3)
Other[A]	1,498 (30.5)
Diagnosed by (n=4,909)	
Physician	2,862 (58.3)
Non-physician	150 (3.1)
Don't know	1,897 (38.6)
At the time of diagnosis, I sought nutritional counseling (n=4,909)	
Yes	1,894 (38.6)
No	1,821 (37.1)
Don't know	1,194 (24.3)
Where do you obtain your primary information about celiac disease? (n=3,276)	
Physician	691 (14.1)
Non-physician healthcare provider	238 (4.9)
Social media/Internet web page	1,371 (27.9)
Other media (book, magazine)	155 (3.2)
Foundation or Support Group	309 (6.3)
Do not use information source	310 (6.3)
Don't know/Other	1,835 (37.4)
Mean CD QOL Score (n=2981, ±SD)	62.5 (13.5)
I am just as healthy as anybody I know (n=679)	
Strongly Disagree	63 (9.3)
Somewhat Disagree	183 (27.0)
Neither Agree or Disagree	134 (19.7)
Somewhat Agree	222 (32.7)
Strongly Agree	77 (11.3)
I keep a strict gluten free diet (n=3,625)	
Always	3,082 (85.0)
Often	393 (10.8)
Sometimes	81 (2.2)
Rarely	34 (0.9)
Never	35 (1.0)
I am still symptomatic despite keeping a Gluten free diet (n=2,456)	
Yes	1,238 (50.4)
No	837 (34.1)
Don't know	381 (15.5)
I use probiotics to aid in the digestion of gluten (n=1,160)	
Yes	381 (32.8)
No	779 (67.2)

Data are presented as N(%) or mean (±SD). [A]Includes: Genetic testing, skin biopsy, gluten challenge, ALCAT food sensitivity test, stool test, allergy skin test, "other" tests.

We compared individuals who responded to the question regarding probiotic use with those who did not (Supplementary file, Table I) and found that respondents had similar age and gender distributions. However, non-respondents were more likely to be younger at the age of diagnosis and less likely to be over the age of 50 years at the time of diagnosis ($p<0.001$). There were also small regional variations in response, with individuals residing in the Midwest being more likely to respond to the probiotics question ($p=0.001$).

We compared patients who reported using probiotics (n=381) to probiotic non-users (n=779) in Table II. There were no significant differences between the two groups in current age, country of origin, or region inhabited. There were significant differences in both age at survey date and age of diagnosis ($p <0.001$ for both comparisons), with probiotic users representing older ages both at the time of survey completion and at diagnosis. There were no differences in the proportion of patients diagnosed by intestinal biopsy ($p=0.23$), serology ($p=0.70$) or using other tests or means of diagnosis ($p=0.10$) and no difference in probiotic use in those diagnosed by a physician versus a non-physician health care practitioner ($p=0.18$). Probiotic use, however, was also more common among those who reported that their primary information source was from a non-physician health care provider (41%) compared to a physician (36%) or those who did not have a primary information source (17%, $p=0.002$). Dietary adherence and self-reported health were similar among probiotic users and non-users.

Responses to the SF-36 scale are shown in Table III. There were no significant differences between the two groups in health change, general health, social functioning, emotional well-being, energy/fatigue, or role limitations due to emotional or physical health. Probiotic users experienced more physical pain (63.7 vs. 69.5, $p=0.006$) and there was a non-significant trend toward reduced physical functioning in probiotic users (84.6 vs. 86.5, $p=0.06$).

We subsequently performed multiple logistic regression analysis, shown in Table IV. After adjustment for all covariates in the model (gender, region, means of diagnosis, primary CD information source, country of origin, whether or not a

Table II. Characteristics of Probiotic Users vs. Probiotic Non-Users

Variable	Probiotic Non-Users (n = 779)	Probiotic Users (n = 381)	p
Gender			
Male	142 (69.6)	62 (30.4)	0.38
Female	630 (66.4)	319 (33.6)	
Age at survey date			
<20	116 (72.1)	45 (28.0)	**<0.001**
20-29	184 (75.7)	59 (24.3)	
30-39	164 (66.9)	81 (33.1)	
40-49	133 (67.5)	64 (32.5)	
50-59	110 (61.8)	68 (38.2)	
≥60	72 (52.9)	64 (47.1)	
Age at diagnosis			
≤10 years old	86 (74.8)	29 (25.2)	**<0.001**
11-19 years old	103 (81.8)	23 (18.3)	
20-29 years old	190 (70.1)	81 (29.9)	
30-39 years old	162 (65.6)	85 (34.4)	
40-49 years old	120 (65.2)	64 (34.8)	
>50 years old	113 (53.6)	98 (46.5)	
US region inhabited			
Northeast	178 (68.2)	83 (31.8)	0.99
South	152 (66.7)	76 (33.3)	
Midwest	206 (66.5)	104 (33.6)	
West	152 (67.3)	74 (32.7)	
Unknown/Outside US	91 (67.4)	44 (32.6)	
Country of origin			
United States	693 (67.1)	340 (32.9)	0.89
Other	86 (67.2)	41 (32.3)	
Means of diagnosis			
Biopsy of the intestine or small bowel during EGD	586 (68.1)	274 (31.9)	0.23
Serology	618 (66.9)	306 (33.1)	0.70
Other	246 (63.9)	139 (36.1)	0.10
Diagnosed by			
Physician	609 (68.7)	277 (31.3)	0.10
Non-physician	22 (57.9)	16 (42.1)	
Unknown	148 (62.7)	88 (37.3)	
Sought nutritional counseling at time of diagnosis			
Yes	357 (63.8)	203 (36.3)	**0.05**
No	411 (70.1)	175 (29.9)	
Don't know	7 (70.0)	3 (30.0)	
Where do you obtain your primary information about celiac disease?			
Non-physician healthcare provider (dietitian, etc)	56 (59.0)	39 (41.1)	**0.002**
Physician	177 (63.9)	100 (36.1)	
Social media/Internet web page	310 (68.9)	140 (31.1)	
Other media (book, magazine)	35 (63.6)	20 (36.4)	
Foundation or Support Group	53 (63.1)	31 (36.9)	
Don't know	47 (61.0)	30 (39.0)	
Do not use information source	101 (82.8)	21 (17.2)	
Mean CD QOL Score (±SD)	62.8 (15.1)	61.6 (15.3)	0.2
I am just as healthy as anybody I know			
Strongly disagree	26 (57.8)	19 (42.2)	0.57
Somewhat disagree	79 (68.1)	37 (31.9)	
Neither agree or disagree	60 (68.2)	28 (31.8)	
Somewhat agree	110 (71.0)	45 (29.0)	
Strongly agree	40 (70.2)	17 (29.8)	
I keep a strict gluten free diet			
Always	668 (66.2)	341 (33.8)	0.087
Often	75 (70.1)	32 (29.9)	
Sometimes	17 (70.8)	7 (29.2)	
Rarely	7 (100)	0 (0)	
Never	12 (92.3)	1 (7.7)	

Table II (continued)

I am still symptomatic despite keeping a gluten free diet			
Yes	329 (59.7)	222 (40.3)	**<0.001**
No	279 (74.8)	94 (25.2)	
Don't know	132 (70.2)	56 (29.8)	

Data are presented as N(%) or mean (±SD). Bolded values are p-values at level of significance <0.05. P-values for difference amongst categories were obtained from Chi-square, Student's T test, or Mann-Whitney U Test.

nutritionist was sought at time of diagnosis, GFD adherence, age at diagnosis, and whether or not patients remain symptomatic despite adherence to a GFD), probiotic users were twice as likely to have been diagnosed over the age of 50 (aOR=2.04, 95%CI: 1.37-3.04) and half as likely to be diagnosed between the ages of 11-19 (aOR=0.50, 95%CI: 0.29-0.85) as compared to those diagnosed between the ages of 20-29. Patients who did not use any primary information source were less likely to use probiotics as compared to those whose physicians served as their primary source of information (aOR=0.42 95%CI: 0.24-0.73). Patients who remained symptomatic despite adherence to a GFD were almost twice as likely to use probiotics (aOR=1.94, 95%CI: 1.44-2.63). Given that few survey participants responded to questions regarding the SF-36 (n=683) we chose to omit the findings from the primary multivariable model. However, when the pain subscale of the SF-36 was incorporated into the model (Supplementary file, Table II), there was an increased likelihood of probiotic use with pain scale sub-scores below 90, with the highest odds of probiotic use (aOR=4.01, 95%CI: 1.44-11.14) in respondents in the lowest quartile (corresponding to scores 0-45, the greatest degree of physical pain experienced).

DISCUSSION

Patients with CD commonly use supplements including probiotics for perceived health benefits. While numerous studies have investigated their use in other gastrointestinal disease, such as inflammatory bowel disease and *Clostridium difficile* infection [14-20], little is known about probiotic use in CD. A recent meta-analysis by Seiler et al. [21] of seven studies, including six randomized controlled trials suggests a statistically significant symptom benefit of probiotic use when measured by the Gastrointestinal Symptom Rating Scale, but not when other questionnaires were employed with evidence certainty rated as very low to low. In this large study of a national CD registry, about one third of CD patients reported using probiotic supplements. We identified three statistically significant predictors of probiotic use on multivariable analysis: age at diagnosis, the persistence of symptoms despite maintaining a GFD, and not reporting a primary information source when learning about CD.

We found that patients diagnosed with CD at age 50 or later were twice as likely to use probiotics. It is possible that this finding simply reflects temporal trends in the general population in which probiotic use has steadily increased since 2007 [8]. Other explanations may be related to the differences in CD presentation with age. Several studies have shown age-related differences in clinical and histological features of CD at initial diagnosis. For example, Vivas et al. [22] demonstrated that the delay between symptom onset and CD diagnosis increases with age, a finding the authors attributed to a lower disease awareness among adult healthcare professionals and the atypical clinical presentation among adults. One possible explanation for our finding may therefore be that patients diagnosed later in life have been symptomatic and/or misdiagnosed for a longer period of time and may be more likely to have tried probiotics or other supplements for relief. Age-related differences in symptom management may also play a role; a large, retrospective study conducted by Jericho et al. [23] found that children adherent to a strict GFD had faster and higher rates of improvement in gastrointestinal and extraintestinal symptoms as compared to adults. The higher use of probiotics among adults diagnosed later in life may therefore be attributed to a greater need for alternative methods of symptom control.

Patients who denied using any information source (such as healthcare providers, online media or support groups) to obtain primary information about CD were significantly less likely to use probiotics than patients who utilized one or more sources. This association may be as a result of the rising popularity of complementary and alternative medical

Table III. SF-36 Scores in Probiotic Users vs. Probiotic Non-Users (n = 683)

SF-36 Scale	Overall Mean (±SD)	Probiotic Non-Users Mean (±D)	Probiotic Users Mean (±D)	p value
Physical functioning	85.9 (18.4)	86.5 (19.9)	84.6 (17.4)	0.06
Role limitations due to physical health	68.2 (39.6)	69.6 (39.5)	64.6 (40.1)	0.19
Role limitations due to emotional health	52.8 (43.4)	54.5 (43.2)	48.4 (42.9)	0.13
Energy/fatigue	43 (20.6)	43.9 (21.7)	41.7 (19.9)	0.28
Emotional well-being	60.9 (17.4)	60.7 (17.8)	62.8 (16.4)	0.29
Social functioning	72.6 (24.1)	73.1 (25.0)	74.2 (23.2)	0.83
Pain	67.1 (21.7)	69.5 (22.1)	63.7 (21.6)	**0.006**
General health	53.6 (22.1)	55.6 (21.9)	52.2 (23.4)	0.13
Health change	58.1 (23.8)	57.6 (22.4)	61.3 (27.4)	0.11

Table IV. Independent predictors of probiotic usage among celiac disease patients*

Variables	OR (95% CI)	p
Gender		
Male	ref	
Female	1.30 (0.91-1.86)	0.14
Age at Diagnosis		
≤10 years old	0.86 (0.50-1.47)	0.58
11-19 years old	0.50 (0.29-0.85)	**0.011**
20-29 years old	ref	--
30-39 years old	1.22 (0.83-1.80)	0.31
40-49 years old	1.27 (0.84-1.93)	0.26
>50 years old	2.04 (1.37-3.04)	**<0.001**
Where do you obtain your primary information about celiac disease?		
Non-physician healthcare provider (i.e. dietician)	1.00 (0.60-1.66)	0.99
Physician	ref	--
Social media/Internet web page	0.74 (0.52-1.04)	0.78
Other media (book, magazine)	0.77 (0.41-1.46)	0.43
Foundation or Support Group	0.90 (0.53-1.54)	0.71
Don't know	1.16 (0.67-2.03)	0.59
Do not use information source	0.42 (0.24-0.73)	**0.002**
At the time of diagnosis, I sought nutritional counseling		
Yes	1.24 (0.95-1.63)	0.12
No	ref	--
Don't know	0.66 (0.13-3.39)	0.61
I am still symptomatic despite keeping a gluten free diet		
Yes	1.94 (1.44-2.63)	**<0.001**
No	ref	--
Don't know	1.18 (0.79-1.78)	0.42

Bolded values are p-values at level of significance <0.05. *This model adjusts for gender, region, means of diagnosis, primary CD information source, country of origin, whether or not a nutritionist was sought at time of diagnosis, GFD adherence, age at diagnosis, and whether or not patients remain symptomatic despite adherence to a GFD.

therapy, and the popularity of the GFD in that field [24]. The fact that those who relied on non-physician health-care providers (including dietitians) were similar to those who relied on physicians for their advice may be due to the central role of the dietitian in the management of CD. It is important to note that the questionnaire in this study did not distinguish whether probiotic use among participants was prescribed or recommended by a physician; that said, a recent study by O'Connor et al. [25] showed that over 65% of probiotic use is self-initiated rather than guided by a physician recommendation.

One important finding in this study is that patients who remain symptomatic despite adhering to a strict GFD are twice as likely to use probiotics as those who achieve symptom resolution. This finding suggests that patients may be seeking additional means of treatment for persistent symptoms. Few human studies have examined the potential for clinical benefit with probiotic use in CD. In an exploratory, randomized controlled trial studying the effects of *Bifidobacterium infantis natren life start* strain on patients with untreated CD, patients in the treatment group experienced a significant improvement in gastrointestinal symptoms compared to controls despite no difference in intestinal permeability [26]. Similarly, a randomized controlled study of a multispecies probiotic mixture of 5 strains of *Lactobacillus* and *Bifidobacterium* revealed an improvement in severity of IBS-type symptoms in CD patients adherent to a strict GFD [27]. Despite these encouraging findings, studies of other strains, including one on *Bifidobacterium longum CECT 7347* and another on VSL #3 (a blend of *Streptococcus*, *Bifidobacterium*, and *Lactobacillus* species) did not demonstrate any significant improvement in symptoms between treatment and control groups [28, 29]. Regardless of any actual benefit, our findings suggest that patients with uncontrolled CD symptoms may perceive probiotics as a potential adjunctive treatment.

To our knowledge, this study is one of the first to investigate the prevalence and predictors of probiotic use among CD patients. Other strengths include the large number of participants (4,909 with 1,160 patients responding to a question regarding probiotic use) and the broad, nationwide scope of the study survey. We also recognize several limitations of this study. First, the study data was obtained from a voluntary survey in a patient-powered research network and is therefore prone to selection bias; participants may have greater self-awareness and attention to their symptoms than the general CD population. Furthermore, as patients who were diagnosed with CD after the age of 50 years were more likely to respond to the question regarding probiotic use, it is possible that there is a selection bias which led to this finding. Our study was also limited to a low number of individuals who responded (24%) to our question of interest regarding probiotic use. This question was added to the survey in August of 2017, more than 18 months after the launch of the PPRN. Therefore, a significant number of participants who filled out the survey prior to

this date did not have the option to answer this question. Quantification of probiotic use (i.e. daily, thrice weekly, etc) was not included in the questionnaire, precluding the ability for a dose-response analysis. Use of self-reported data in this study, particularly self-reported CD status, also limits the generalizability and internal validity of its findings given that the data is only as accurate as the participant's ability to recall prior events. Additionally, the retrospective design of this study limits the ability to draw conclusions about whether probiotic use itself has any effect on symptoms or quality of life and as we did not correct for multiple comparisons, the significant findings in this cross-sectional analysis should be regarded as hypothesis-generating.

CONCLUSIONS

This analysis of data obtained through a national CD registry demonstrated that probiotic use is common among patients with CD and is associated with older age at diagnosis. Those who remained symptomatic despite a GFD were twice as likely to take probiotics, compared with those reporting symptom control. Patients who reported the most pain were also the most likely to take probiotics. These findings suggest that patients may be seeking additional means of treatment for persistent symptoms. Further study is needed to clarify whether or not these symptoms are related to accidental gluten ingestion and to evaluate any benefit of using probiotics in symptoms or quality of life in people with CD.

Conflicts of interest: None to declare.

Authors' contributions: A.M.J., B.L., M.G., P.H.G. conceived and designed the study. A.M.J., R.M.C. collected data. A.M.J., J.W.B. analyzed data. AMJ, AMC drafted the manuscript. AMJ, A.M.C., M.G., J.W.B., R.M., B.L., P.H.G. revised the manuscript.

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