

# The Virtual Celiac Symptoms Study: symptom and gluten-free diet perceptions at baseline

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## Introduction

- Celiac disease (CeD) is a chronic, immune-mediated, systemic disorder characterized by inflammation of the small intestine and serological changes in response to gluten ingestion. Patient groups with distinct symptom patterns/burden profiles are not clearly defined.<sup>1,2</sup>
- A gluten-free diet (GFD) is the only current management option for CeD but requires strict adherence, which can be burdensome, and some patients continue to experience symptoms owing to inadvertent gluten exposure.<sup>2-6</sup>
- There is substantial heterogeneity in the clinical manifestations of CeD and the impact of CeD on patients' quality of life (QoL) is not well understood.<sup>1,5</sup>
- The Virtual Celiac Symptoms Study is the first longitudinal study to assess daily symptom patterns and impacts of CeD in US adults and adolescents.

## Objective

- To describe the baseline disease characteristics of the adult study population of the Virtual Celiac Symptoms Study.

## Methods

### Study design

- The Virtual Celiac Symptoms Study (NCT05309330) is an observational, prospective study conducted in US adult and adolescent patients with CeD.
- The study collected data from patients for 12 weeks, with daily collection of symptoms (Celiac Disease Symptom Diary v2.1; CDSD v2.1) and known and suspected inadvertent gluten exposure, weekly assessment of healthcare resource utilization and missed work and school, and periodic assessments using other instruments, including the EQ-5D questionnaire, 12-item Short-Form Health Survey (SF-12), Work Productivity and Activity Impact Questionnaire (WPAI) and QoL impacts.<sup>8-10</sup>
- All data were self-reported and collected via a smart phone app.
- Patients were recruited by the Celiac Disease Foundation via digital advertisements (email, social media channels, app push notifications, website ads and a study microsite).
- Data collection began on July 25, 2022 and ended on March 4, 2023.

### Inclusion criteria

- English-speaking US citizens aged at least 12 years
- Diagnosis of CeD for at least 1 year, confirmed via self-reported biopsy and serology
- Adherence to a GFD for at least 6 months
- CeD-related symptoms (patient-reported) within the past 3 months
- Daily access to a smartphone and internet/Wi-Fi/cellular data

### Exclusion criteria

- Planned or current involvement in any clinical study with an investigational drug, or surgical procedure or gluten challenge during the 3-month observation period.

### Data analysis

- Analysis of findings over the 12-week observation period is ongoing.
- All baseline measures were analyzed using descriptive statistics.

## Results

### Patient demographics and clinical disease characteristics

- The baseline questionnaires were completed by 338 adult patients (**Table 1**).
- The mean (standard deviation; SD) age was 37.9 (12.5) years, 87.9% were female and 98.5% were White.
- Overall, 84.9% of patients reported that they received a CeD diagnosis at age 18 years or older, 10.9% at age 12-17 years, 3.6% at age 6-11 years and 0.6% at age younger than 6 years.
- Mean (SD) duration of disease since CeD diagnosis was 7.3 (5.3) years, and mean (SD) duration between first gluten-related symptom of CeD and CeD diagnosis was 8.0 (9.8) years.
- The most common comorbidities (> 40.0%) were anxiety, headache and depression (**Table 1**).

**Table 1.** Baseline demographics and clinical disease characteristics

	Adult patients (N = 338)
<b>Age, years, median (range)</b>	37 (18-71)
<b>Duration of adherence to a GFD, years, mean (SD)</b>	7.1 (5.0)
<b>Education, n (%)</b>	
Advanced degree	118 (34.9)
College graduate (Bachelor's degree)	105 (31.1)
Some college or associate's degree	92 (27.2)
High school, junior high/middle or elementary	23 (6.8)
<b>Comorbidities, n (%)</b>	
<b>Gastrointestinal conditions</b>	
Gastroesophageal reflux disease	86 (25.4)
Irritable bowel syndrome	70 (20.7)
Small intestinal bacterial overgrowth	18 (5.3)
Microscopic colitis (lymphocytic or collagenous colitis)	14 (4.1)
Gastroparesis/delayed gastric emptying	9 (2.7)
Ulcerative colitis	5 (1.5)
Crohn's disease	4 (1.2)
<b>Autoimmune conditions</b>	
Thyroid disease	70 (20.7)
Type 1 diabetes	6 (1.8)
Sjogren's syndrome	4 (1.2)
Rheumatoid arthritis	3 (0.9)
<b>Mental health</b>	
Anxiety	192 (56.8)
Depression	143 (42.3)
Attention deficit hyperactivity disorder	51 (15.1)
<b>Skin conditions</b>	
Dermatitis herpetiformis	44 (13.0)
<b>Neurological conditions</b>	
Headache	156 (46.2)
Headache diagnosed as migraine	102 (65.4) <sup>a</sup>
Peripheral neuropathy	26 (7.7)
Ataxia	6 (1.8)
<b>Miscellaneous</b>	
Anemia	68 (20.1)
Osteoporosis/osteopenia	31 (9.2)
Chronic fatigue syndrome	17 (5.0)
Fibromyalgia	17 (5.0)
Postural orthostatic tachycardia syndrome	15 (4.4)
Hypertension	9 (2.7)
Asthma	8 (2.4)
Type 2 diabetes	7 (2.1)
Cancer of any type	7 (2.1)
Polycystic ovary syndrome	5 (1.5)
Ehlers-Danlos syndrome	5 (1.5)
High cholesterol	5 (1.5)
Eosinophilic esophagitis	4 (1.2)
Other <sup>b</sup>	71 (21.0)
<b>Failure to thrive as a small child or difficulty gaining weight at any point</b>	
Yes	67 (19.8)
No	240 (71.0)
Unknown/not sure	31 (9.2)

GFD, gluten-free diet; SD, standard deviation.

<sup>a</sup>Percentage of patients reporting headache.

<sup>b</sup>Other miscellaneous comorbidities included adrenal insufficiency, allergic rhinitis, ankylosing spondylitis, bipolar disorder, breast fibroadenoma, IgA deficiency, obstructive sleep apnea and vitiligo.

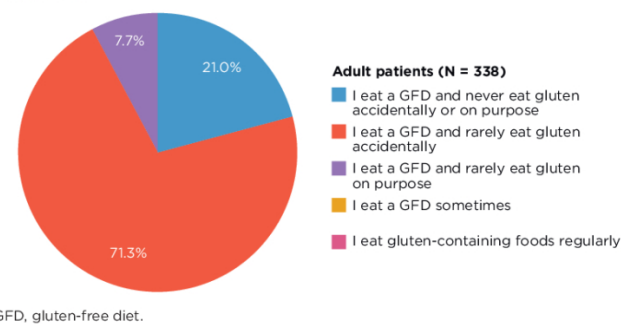
### GFD adherence and dietary assessment

- All patients reported adhering to a GFD (**Figure 1**).
  - Most patients reported "rarely eating gluten accidentally".
  - The remaining patients reported "never eating gluten accidentally or on purpose" or "rarely eating gluten on purpose".
  - None of the patients reported "eating a gluten-free diet sometimes" or "eating gluten-containing foods regularly".
- In addition to gluten, 32.5% of patients reported having food allergies or intolerances and 34.0% reported additional dietary restrictions (**Table 2**).

## Key messages

- Patients with celiac disease (CeD) report disease-related symptoms despite strictly adhering to a gluten-free diet (GFD).
- This observational study highlights an unmet need for new treatments for patients with CeD on a GFD.

**Figure 1.** Use of GFD by adult patients in the Virtual Celiac Symptoms Study at baseline



GFD, gluten-free diet.

**Table 2.** Food allergies, intolerances and dietary restrictions

	Adult patients (N = 338)
<b>Food allergies or intolerances other than gluten, n (%)</b>	
Yes	110 (32.5)
No	228 (67.5)
<b>Additional dietary restrictions other than gluten, n (%)</b>	
Lactose-free/dairy-free/milk-free	68 (20.1)
Vegetarian	22 (6.5)
Low FODMAP	20 (5.9)
Paleo	6 (1.8)
Vegan	5 (1.5)
Other <sup>a</sup>	33 (9.8)
No dietary restrictions	223 (66.0)
<b>Living with anyone who has been diagnosed with CeD and adheres to a GFD, n (%)</b>	
Yes	45 (13.3)
No	290 (85.8)
Unknown/not sure	3 (0.9)

CeD, celiac disease; FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides and polyols; GFD, gluten-free diet.

<sup>a</sup>Dietary restrictions other than gluten include bariatric diet, tree nut-free, egg-free, kosher, low caffeine, low carb/low fiber, low fat, low sodium, low sugar, no artificial sweeteners, no banana, no coconut, no corn, no peanut, no pork/pork products, no shellfish, oat-free, pescatarian and soy-free.

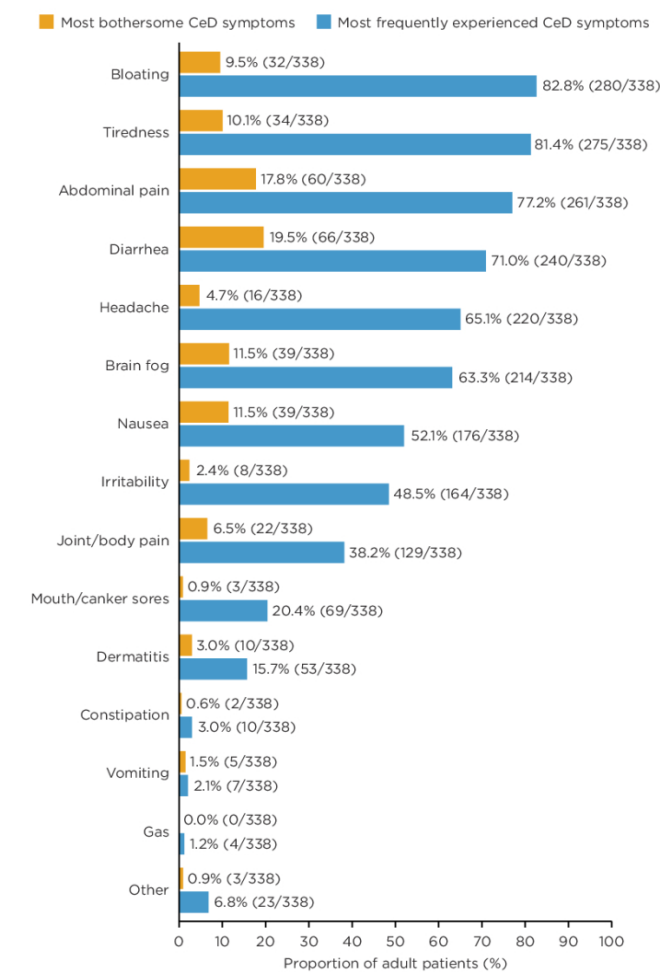
### CeD symptom profile

- CeD-related symptoms were reported by 58.3%, 31.1% and 10.7% of patients in the past week, past month and past 3 months, respectively.
- The top four most commonly reported symptoms were bloating, tiredness, abdominal pain and diarrhea, and the most bothersome symptoms were diarrhea, abdominal pain, brain fog and nausea (**Figure 2**).
- Almost all patients surveyed (96.4%) reported occurrence of CeD symptoms, with almost a quarter indicating that they experienced symptoms despite not having been knowingly exposed to gluten (**Figure 3**).
- In total, 84.0% of patients reported that they were likely/extremely likely to experience CeD symptoms after gluten exposure.
- Over 70.0% of patients described symptom intensity as moderate (38.5%) or severe (32.5%). The remaining patients reported mild symptom severity (5.6%) or had varying levels of symptom severity (23.4%).

### Healthcare resource utilization

- In total, 11.0% of patients reported hospitalization or emergency room (ER) visits due to CeD symptoms in the past year.
- Urgent care facility visits, ER visits or hospitalization due to CeD symptoms after gluten exposure was reported as "never" by 87.0% of patients, "sometimes" by 11.8% or "always" by 1.2%.

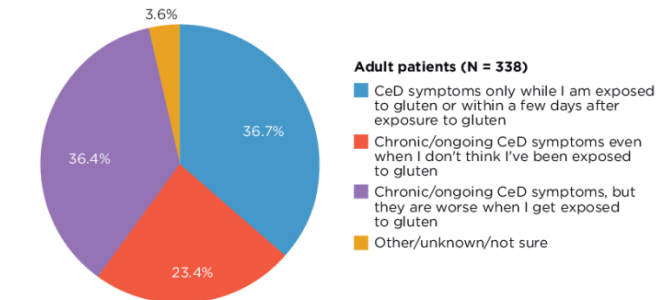
**Figure 2.** The most frequent and most bothersome symptoms of CeD experienced by adult patients in the Virtual Celiac Symptoms Study at baseline



CeD, celiac disease. Data next to bars represent % (n/N).

For frequently experienced symptoms, "other" included acid reflux, anxiety, blurry vision, body aches from chest through stomach, boils on stomach, depression, dizziness, dry eyes, goopy stools, hair falling out, heartburn, hives, inner ear pain, lack of appetite, light headedness, peripheral neuropathy and tingy fingertips. For bothersome symptoms, "other" included depression, dizziness, light headedness and sun sensitivity.

**Figure 3.** Occurrence of CeD symptoms in adult patients in the Virtual Celiac Symptoms Study at baseline



CeD, celiac disease.

## Limitations

- Patient eligibility was based on a self-reported confirmed diagnosis of CeD; therefore, there may have been misclassification of some CeD diagnoses.
- Self-reporting of gluten intake is subjective and liable to inaccuracies.
- The study population may not be representative of all US patients with CeD, because this sample was recruited through advocacy organization channels.
  - Patients with CeD who follow an advocacy organization or subscribe to newsletters are likely better informed about their disease and may be more compliant with their disease management.
- The experience among patients with CeD in countries other than the USA may differ. However, a previous study in patients from the UK, Spain and Germany in addition to the USA reported similar observations.<sup>10</sup>
- The results presented here may not be representative of children and adolescents with CeD; however, this study also includes an adolescent cohort and their CeD experiences will be evaluated in future analyses.

## Conclusions

- Despite high levels of reported adherence to a GFD, many patients still report CeD-related symptoms, especially in response to perceived gluten exposure.
- More than two-thirds of patients reported their symptoms as moderate or severe, and over a tenth of patients reported a CeD-related hospitalization or ER visit in the past year.
- Ongoing analyses of the adult study population will characterize the symptom and GFD patterns, QoL impacts and healthcare resource utilization over the 12-week observation period.
- This study supports the need for further understanding of persistent/recurrent symptoms and additional treatments for patients with CeD on a GFD.

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