

# Adherence to the gluten-free diet and celiac disease patient outcomes: real world evidences from an international patient registry, iCureCeliac®

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## Background

- Celiac disease (CeD) is a chronic, multisystem autoimmune disease of the small intestine, in which ingestion of dietary gluten triggers an inflammatory response in genetically susceptible individuals.
- The incidence of CeD in Europe and the USA has been estimated at between 11.8 and 17.4 per every 100,000 persons per year,<sup>1,2</sup> consistent across adults and children (<16 years of age).
- Globally, the prevalence of CeD was shown to be 0.5–1%.<sup>3,4</sup>
- At present, the only option for patients with CeD is a strict, lifelong adherence to a gluten-free diet (GFD), which involves complete avoidance of proteins from wheat, barley, and rye.
- Few studies have evaluated GFD adherence and its association with patient outcomes.

## Study objectives

- To assess the real-world adherence to GFD in patients with CeD and the associated patient outcomes.

## Methods

- A retrospective cohort analysis (Figure 1).

### Data source

- iCureCeliac®, founded in 2016 by the Celiac Disease Foundation, is an online registry for patients to provide self-reported critical insights into living with CeD, including information on:



### Diagnostic journey and current monitoring of CeD

- Tests to confirm diagnosis, reason for diagnosis (e.g. symptomatic)
- Number and type of healthcare professionals (HCPs) seen and diagnostic delay
- Current disease management and frequency of visits



### Adherence to the GFD and treatment preferences

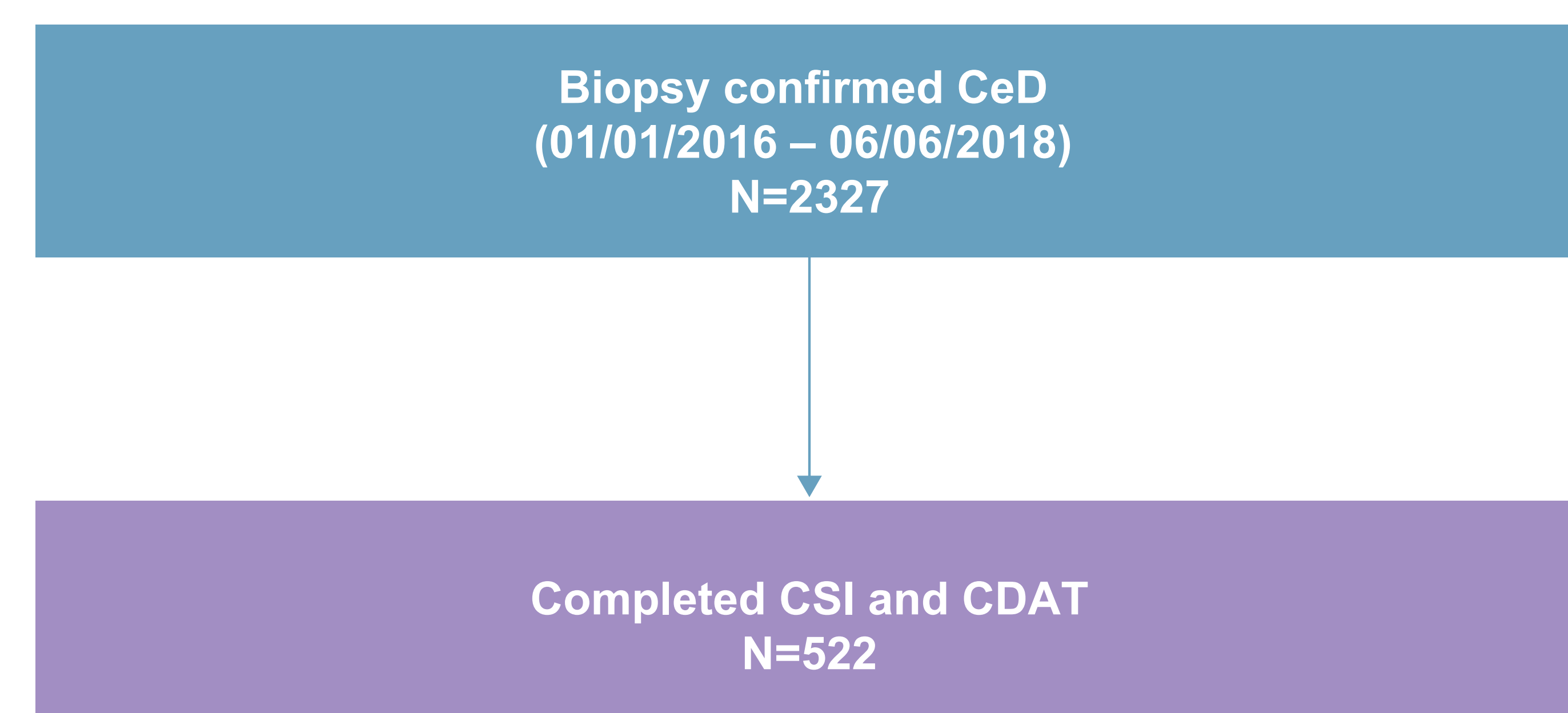
- Self-rated “strict GFD” and validated measure of adherence
- Frequency of inadvertent and intentional gluten exposure
- Interest in hypothetical treatments based on route of admission, frequency, and cost



### Quality of life and burden of disease

- A patient-reported outcome (PRO) measure of quality of life provides a validated metric of the burden of CeD
  - Celiac Symptoms Index (CSI), Celiac Dietary Adherence Test (CDAT), Celiac Disease Quality of Life Measure (CD-QOL), SF-36, Patient-Reported Outcomes Measurement Information System (PROMIS) Gastrointestinal, PROMIS 29 Profile, and PROMIS Pediatric 25 Profile
- Impact on activities of daily living and social interactions
- Number of work/school days missed owing to CeD.

Figure 1. Study cohort



CDAT, Celiac Dietary Adherence Test; CeD, celiac disease; CSI, Celiac Symptoms Index

## Results

- A high proportion of patients registered with the iCureCeliac registry were female (Table 1). **The registry may therefore be over-representative of female patients with CeD.**
- The registry is geographically diverse** – it represents patients throughout the USA (Table 1).
- A total of **115 patients (22.1%) chose self-management only.**
- The primary reason for diagnosis was the **presence of symptoms (75.1%)**, followed by a request for screening by a HCP (30.9%). Other reasons included:
  - a family member with CeD (12.3%)
  - another autoimmune disease (12.3%)
  - a request for screening (9.4%).
- More than half of the patients (55.4%) had three or more HCP visits for gluten-related disorder prior to their CeD diagnosis (Figure 2).
- Only 24.1% of the patients had symptomatic control over their disease, i.e. low disease symptom burden, while about one third of patients still had high disease burden (CSI≥45) (Table 3).

Table 1. Patient demographic and baseline characteristics

Female, n (%) (N=521)	425 (81.6%)
Mean age when first diagnosed with gluten-related disorder, years (SD) (N=514)	31.3 (17.2)
Mean time since CeD diagnosis, months (SD) (N=519)	60.9 (84.2)
Mean age, years (SD) (N=521)	35.9 (17.3)
Age categories, n (%) (N=521)	
Less than 15 years	71 (13.6%)
15–40 years	238 (45.7%)
41–65 years	191 (36.7%)
Over 65 years	21 (4.0%)
Race and ethnicity, n (%) (N=514)	
White	486 (94.6%)
Hispanic	26 (5.1%)
Geographic region, n (%) (N=452)	
Northeast	121 (26.8%)
Midwest	141 (31.2%)
South	98 (21.7%)
West	92 (20.4%)

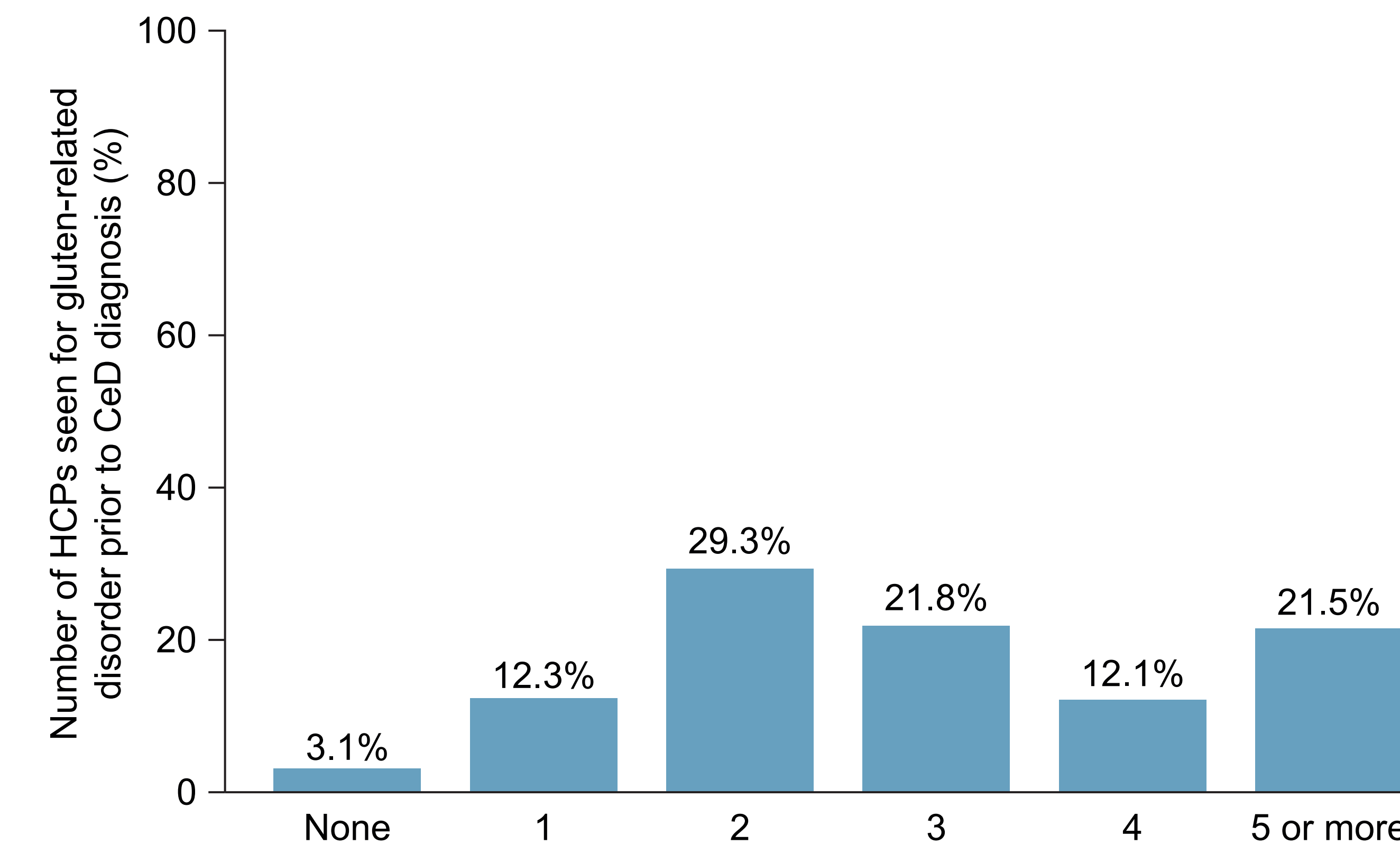
CeD, celiac disease; SD, standard deviation

Table 2. Specialty of HCPs managing the gluten-related disorder (N=521), n (%)

Self-managed	262 (50.3%)
Gastroenterologist	252 (48.4%)
Family Medicine Practitioner	139 (26.7%)
Pediatric Gastroenterologist	40 (7.7%)
Pediatrician	39 (7.5%)
Dietitian	33 (6.3%)
Internist	26 (5.0%)
Nutritionist	25 (4.8%)
Other HCP	22 (4.2%)
Endocrinologist	19 (3.7%)
Naturopath	11 (2.1%)
Chiropractor	10 (1.9%)
Rheumatologist	9 (1.7%)
Not managed	9 (1.7%)
Management is not required	8 (1.5%)
Pediatric Endocrinologist	4 (0.8%)

HCP, healthcare professional

Figure 2. Number of HCPs seen for gluten-related disorder prior to CeD diagnosis



CeD, celiac disease; HCP, healthcare professional

- Half of patients (50.2%) had excellent GFD adherence based on CDAT score (CDAT ≤ 12), with the majority (96.4%) of patients reporting that they “always” or “often” maintained a strict GFD in a single question in the CDAT.
  - There was a large discrepancy between self-reported and PRO measures of GFD adherence.
- Among those with excellent adherence to a GFD (CDAT ≤ 12), low disease symptomatic control (CSI≤30) was achieved in 41.2% of patients and high disease symptom burden (CSI≥45) persisted in 9.2% of patients (Table 3).
- The majority of those with poor GFD adherence (CDAT>16) experienced high disease symptom burden (63.3% with CSI≥45), and no one achieved low disease symptomatic control (CSI≤30) (Table 3).
- Quality of life was significantly higher in those with low disease symptom burden (mean [standard deviation]: 72.0 [12.0]) compared with either moderate disease symptom burden (61.0 [13.2]) (p<0.0001) or high disease symptom burden (54.0 [12.5]) (p<0.0001) (Table 4).
- Patients with high disease symptom burden (CSI≥45) missed on average more than 5 weeks of work or school per year due to illness-associated gluten exposure. This was significantly more than the number of missed work or school days in patients with either moderate (31≤CSI≤44) (p=0.0003) or low disease symptom burden (CSI≤45) (p<0.0001) (Table 4).
- Even for patients with excellent GFD adherence (CDAT≤12), on average 3 weeks of work or school in a year were missed for those with high disease symptom burden (CSI≥45) (Table 5).
- Patients with poor adherence to GFD (CDAT>16) had more work or school absenteeism per year than those with excellent adherence to GFD (CDAT≤12) (p=0.0033) (Table 5).

Table 3. Symptom burden among those with sufficient or insufficient GFD adherence, based on CSI and CDAT scores

Celiac Symptom Index (CSI)	Overall (n=522)	Excellent adherence to GFD (CDAT≤12) (n=262)	Fair adherence to GFD (13≤CDAT≤16) (n=181)	Poor adherence to GFD (CDAT>16) (n=79)
Low disease symptom burden (CSI≤30)	126 (24.1%)	108 (41.2%)	18 (9.9%)	n/a
Moderate disease symptom burden (31≤CSI≤44)	239 (45.8%)	130 (49.6%)	80 (44.2%)	29 (36.7%)
High disease symptom burden (CSI≥45)	157 (30.1%)	24 (9.2%)	83 (45.9%)	50 (63.3%)

CDAT, Celiac Dietary Adherence Test; GFD, gluten-free diet

Table 4. Quality of life and annual work/school days missed by levels of disease symptom burden

Celiac Symptom Index (CSI)	Celiac Disease Quality of Life (CD-QOL), mean (SD)	Annual work/school days missed owing to gluten exposures, mean (SD)
Low disease symptom burden (CSI≤30) (n=126)	72.0 (11.9) (n=121)	5.7 (7.1) (n=39)
Moderate disease symptom burden (31≤CSI≤44) (n=239)	61.0 (13.2) (n=230)	12.0 (24.2) (n=129)
High disease symptom burden (CSI≥45) (n=157)	54.0 (12.5) (n=148)	37.1 (68.4) (n=112)

SD, standard deviation

- Most patients understood that accidental exposure to gluten had a negative impact on their health, however, 74% had **accidental gluten exposure in the last 30 days.**
- Despite excellent adherence to a GFD (CDAT≤12); **62.1% of patients with CeD still had accidental exposure in the past 30 days.**

Table 5. Annual work/school days missed by levels of disease symptom burden and adherence to GFD

Celiac Symptom Index (CSI)	Excellent adherence to GFD (CDAT≤12) (n=262)	Fair adherence to GFD (13≤CDAT≤16) (n=181)	Poor adherence to GFD (CDAT>16) (n=79)
Low disease symptom burden (CSI≤30) (n=126)	5.6 (7.3) (n=35)	7.0 (5.5) (n=4)	n/a
Moderate disease symptom burden (31≤CSI≤44) (n=239)	7.2 (11.2) (n=64)	15.3 (28.7) (n=52)	22.5 (42.1) (n=13)
High disease symptom burden (CSI≥45) (n=157)	21.3 (36.2) (n=18)	39.0 (75.9) (n=58)	42.1 (68.4) (n=36)

CDAT, Celiac Dietary Adherence Test; GFD, gluten-free diet

## Study limitations

- Selection bias may exist as patients self-selected to report in the registry and complete the PRO measures.
- Diagnosis of CeD was not verified by clinicians.

## Conclusions

- Self-perceived adherence to a GFD can be misleading as it almost doubles what is measured by a validated instrument.
- Half of the patients with CeD in this study were unable to effectively adhere to a GFD.
- Symptom burden is strongly and inversely correlated with quality of life.
- Despite adherence to a GFD, many patients still had persistent high symptom burden and reduced quality of life.
- Inadvertent gluten exposure results in significant loss of productivity.
- The evidence suggests that adhering to a GFD is not universally effective at decreasing symptom burden and there is a significant unmet need for better treatment options.

## References

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## Disclosures

KR, SW and DL are employees of Takeda Pharmaceutical International. JD was employed by Takeda Pharmaceutical International when this research was conducted. MG is the chief executive officer of the Celiac Disease Foundation and provided consultancy services for Takeda.

## Acknowledgments

This study was sponsored by Takeda Pharmaceutical Company Ltd. Editorial assistance was provided by Oxford PharmaGenesis.