Diagnosing Celiac Disease in the United States of America, Germany, Italy and Spain: Findings from a Real-World Survey

***Authors**: Fatima Dawod[1], Hannah Knight[1], Sophie Barlow[1], Niamh Harvey[1], Grace O'Neill[1], Rina Lukanova[1], Marilyn Geller[2]*

***Affiliations:** [1]Adelphi Real World, Bollington, UK; [2]Celiac Disease Foundation, Woodland Hills, CA, USA*

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Introduction: Late diagnosis of celiac disease (CeD) can lead to long-term health complications and other autoimmune disorders, which may be prevented if managed sooner. Differences in diagnosis of CeD across countries have not been widely researched. We aimed to assess diagnosis patterns in the United States of America (USA) and Europe.

Materials and methods: Data were collected using the Adelphi CeD Disease Specific Programme™,[1-3] a real-world cross-sectional survey with elements of retrospective data collection of physicians and their CeD patients, conducted in the USA, Germany, Italy, and Spain between Jul 2021-Jan 2022. Physicians completed patient record forms for their next 8 consulting adult CeD patients who were symptomatic within the last 12 months, capturing delayed diagnosis, misdiagnosis, and tests to diagnose. The same patients were invited to complete a patient self-completion form capturing consultation history and awareness of CeD prior to diagnosis. Pairwise analysis was used to compare outcomes between countries using Bonferroni corrected t-tests and Fisher's exact test ($\alpha=0.05/6=0.0083$).

Results: The analysis included 2,244 CeD patients (mean age 36.7; female 62%). Patients waited a median of 3-6 months before seeing a physician after symptom onset, with the shortest time taken in Germany; the main reason for this delay was due to patients waiting to see if their symptoms would subside (USA 71%, Germany 85%, Italy 63%, Spain 61%). There was a further delay of 1-3 months from initial consultation to diagnosis, most commonly due to waiting for tests. Over a third of patients were initially misdiagnosed, most commonly with irritable bowel syndrome (84% USA). Circumstances leading to diagnosis varied across countries: Symptom presentation was the most prevalent overall; CeD screening program was significantly higher in Italy than all other countries (18%) and patient request to be tested was significantly lower in Germany (5%), likely due to the low patient awareness of CeD prior to diagnosis (USA 47%, Germany 14%, Italy 56%, Spain 56%). All diagnostic tests were used significantly less in the USA compared to the other countries **(Table 1)**.

Discussion: We found that patients in the USA, Germany, Italy, and Spain experienced long delays in their diagnosis of CeD and were frequently misdiagnosed, with the greatest disparity observed between the USA and Germany. Future research is needed to determine the impact of delayed diagnosis on further health complications and patient outcomes in CeD.

Bibliography:

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Table 1: Physician- and patient reported diagnosis and misdiagnosis of CeD by country

	Country			
	USA[U]	Germany[G]	Italy[I]	Spain[S]
Time between experiencing symptoms and seeing a physician[1], months*	**n=252**	**n=245**	**n=117**	**n=229**
Median (IQR)	6.0 (3.0, 12.0)[G]	3.0 (1.4, 6.0)[ISU]	5.8 (1.0, 12.0)[G]	6.0 (2.0, 12.0)[G]
Top reason for delay between experiencing symptoms and seeing a physician[1]*	**n=266**	**n=258**	**n=121**	**n=235**
I waited to see if my symptoms would go away on their own, n (%)	189 (71.1)[G]	220 (85.3)[ISU]	76 (62.8)[G]	144 (61.3)[G]
Time from first consultation to diagnosis[2], months	**n=537**	**n=416**	**n=335**	**n=395**
Median (IQR)	1.0 (0.3, 3.1)	2.0 (0.9, 4.8)	2.0 (1.0, 5.1)	3.1 (1.1, 7.1)
Top three reasons for delay between first consultation and diagnosis[3]	**n=274**	**n=280**	**n=256**	**n=325**
Waiting for tests, n (%)	146 (53.3)[GS]	74 (26.4)[ISU]	159 (62.1)[GS]	248 (76.3)[GIU]
Waiting for specialist referral, n (%)	69 (25.2)[GIS]	135 (48.2)[U]	112 (43.8)[U]	136 (41.8)[U]
Waiting for test results, n (%)	87 (31.8)[G]	35 (12.5)[ISU]	71 (27.7)[GS]	131 (40.3)[GI]
Patient ever misdiagnosed[2]	**n=638**	**n=448**	**n=380**	**n=421**
Yes, n (%)	205 (32.1)[I]	145 (32.4)	155 (40.8)[U]	150 (35.6)
Top three misdiagnoses[4]	**n=204**	**n=145**	**n=155**	**n=150**
Irritable bowel syndrome, n (%)	172 (84.0)[GIS]	103 (71.0)[U]	99 (64.0)[U]	107 (71.0)[U]
Lactose intolerance, n (%)	50 (25.0)	47 (32.0)	44 (28.0)	34 (23.0)
Gastro-esophageal reflux disease, n (%)	27 (13.0)	11 (8.0)	28 (18.0)	23 (15.0)
Circumstances leading to patient diagnosis[2]	**n=742**	**n=465**	**n=464**	**n=469**
Presenting with symptoms, n (%)	601 (81.0)	403 (86.7)	385 (83.0)	377 (80.4)
Tests for other disease, n (%)	101 (13.6)	70 (15.1)	75 (16.2)[S]	45 (9.6)[I]
CeD screening program, n (%)	37 (5.0)[IS]	18 (3.9)[I]	82 (17.7)[GSU]	9 (1.9)[IU]
Testing due to family history/genetic testing, n (%)	107 (14.4)[GI]	26 (5.6)[SU]	39 (8.4)[SU]	80 (17.1)[GI]
Patient request to be tested for CeD, n (%)	94 (12.7)[G]	21 (4.5)[ISU]	49 (10.6)[G]	47 (10.0)[G]
Tests used to diagnose CeD[5]	**n=739**	**n=438**	**n=441**	**n=468**
Serology tests, n (%)	565 (76.5)[GIS]	380 (86.8)[IU]	418 (94.8)[GU]	425 (90.8)[U]
Imaging tests, n (%)	512 (69.3)[GIS]	372 (84.9)[U]	359 (81.4)[U]	390 (83.3)[U]
Biopsies, n (%)	507 (68.6)[GIS]	358 (81.7)[U]	342 (77.6)[SU]	400 (85.5)[IU]
Were you aware of CeD before you were diagnosed?[1]*	**n=287**	**n=263**	**n=133**	**n=251**
Yes, n (%)	136 (47.4)[G]	36 (13.7)[ISU]	75 (56.4)[G]	140 (55.8)[G]

[GISU]Superscript letters indicate pairwise significant differences between columns with Bonferroni corrections (α=0.05/6=0.0083).

Data reported by physicians unless otherwise specified.
**Indicates patient-reported data.*
[1]Voluntary patient self-completion data.
[2]Patients with known data.
[3]Patients who experienced a delay between consultation and diagnosis.
[4]Patients ever misdiagnosed.
[5]Serology: IgA-EMA, tTG-IgA, genetic testing; Imaging tests: Endoscopy, video capsule endoscopy, gastroscopy, double balloon enteroscopy, colonoscopy, ultrasound, CT scan, MRI, X-ray, bone density scan; Biopsies: duodenum, jejunum, ileum, location unknown.
CeD, celiac disease; CT scan, computerized axial tomography; IgA-EMA, immunoglobin A endomysial antibodies; IQR, interquartile range; MRI, magnetic resonance imaging; tTG-IgA, tissue transglutaminase immunoglobin A; USA, United States of America.

Keywords: Celiac disease, patient care management, delayed diagnosis, type iv hypersensitivity, misdiagnosis