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

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

[1]Adelphi Real World, Bollington, United Kingdom
[2]Celiac Disease Foundation, Woodlands Hills, CA, United States of America

BACKGROUND

- Late diagnosis of celiac disease (CeD) can lead to long-term health complications and other autoimmune disorders, which may be prevented if managed sooner[1].
- Differences in the diagnosis of CeD across countries have not been widely researched.
- We aimed to assess diagnosis patterns in the United States of America (US) and three European countries.

OBJECTIVE

To identify differences in the diagnosis of CeD within the US, Germany (DE), Italy (IT) and Spain (ES).

CONCLUSIONS

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

References:
[1]Norstrom F, et al., BMC Gastroenterol. 2011;7;11:118
[2]Anderson P, et al., Cur Med Res Opin. 2008;24(11):3063-72
[3]Babineaux SM, et al., BMJ Open. 2016;6(8):e010352
[4]Higgins V, et al., Diabetes Metab Syndr Obes. 2016;1(9):371-380
[5]StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC

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METHODS

- Data were drawn from the Adelphi Real World CeD Disease Specific Programme (DSP)™, a cross-sectional survey with retrospective data collection of physicians and their patients with CeD, conducted in the US, Germany, Italy and Spain between July 2021 and January 2022. The DSP methodology has been previously published and validated[2-4].
- Gastroenterologists (GIs) and primary care physicians (PCPs) were recruited to complete patient record forms for their next eight consulting adult CeD patients who were symptomatic in the last 12 months.
- Physicians reported time to diagnosis, reasons for delayed diagnosis, misdiagnosis, events leading to diagnosis and tests used to diagnose.
- The same patients were invited to complete a voluntary patient self-completion form which captured 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, performed using Stata 17[5].
- Significance was observed at α=0.0083 (0.05/6) to adjust for multiple testing.
- Superscript letters ([UDIE]) indicate pairwise significant differences between countries amongst outcomes with Bonferroni corrections (p<0.0083).

RESULTS

Symptom onset to consultation

Overall, 278 physicians (178 GIs, 100 PCPs) reported data on 2,244 patients with CeD in the US, Germany, Italy and Spain, described in **Table 1**.

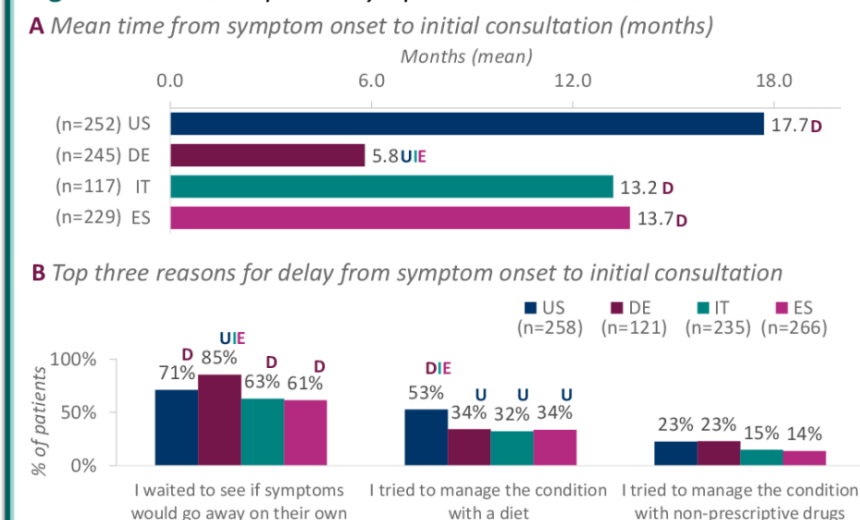Patient self-reported data was collected from 289 (US), 266 (DE), 135 (IT) and 251 (ES) patients.

Table 1. *Patient demographics*

	US	DE	IT	ES
n	**792**	**488**	**483**	**481**
Age, years, mean (SD)	39.8 (14.6)	33.7 (11.0)	35.0 (13.4)	36.3 (13.9)
Sex, n (%)				
Female	499 (63.0)	289 (59.2)	304 (62.9)	307 (63.8)
BMI, mean (SD)	25.6 (4.6)	22.9 (3.1)	24.8 (34.0)	23.3 (3.2)
Smoking status, n (%)				
Current smoker	54 (6.8)	79 (16.2)	107 (22.2)	65 (13.5)
Employment status*, n (%)				
Full-time	478 (60.4)	310 (63.5)	243 (50.3)	224 (46.6)
Student	106 (13.4)	84 (17.2)	129 (26.7)	104 (21.6)
Part-time	96 (12.1)	48 (9.8)	41 (8.5)	42 (8.7)

Top three. SD, standard deviation; BMI, body mass index; US, United States of America; DE, Germany, IT, Italy; ES, Spain.

Patients waited a mean [SD] of 17.7 [43.9] (US), 5.8 [9.3] (DE), 13.2 [26.4] (IT) and 13.7 [21.8] (ES) months before seeing a physician after symptom onset, significantly lowest in Germany (**Figure 1a**). The main reason for this delay was patients waiting to see if their symptoms would subside, most commonly observed in Germany. This was followed by patients trying to manage their condition with a diet, which was significantly more common in the US (**Figure 1b**).
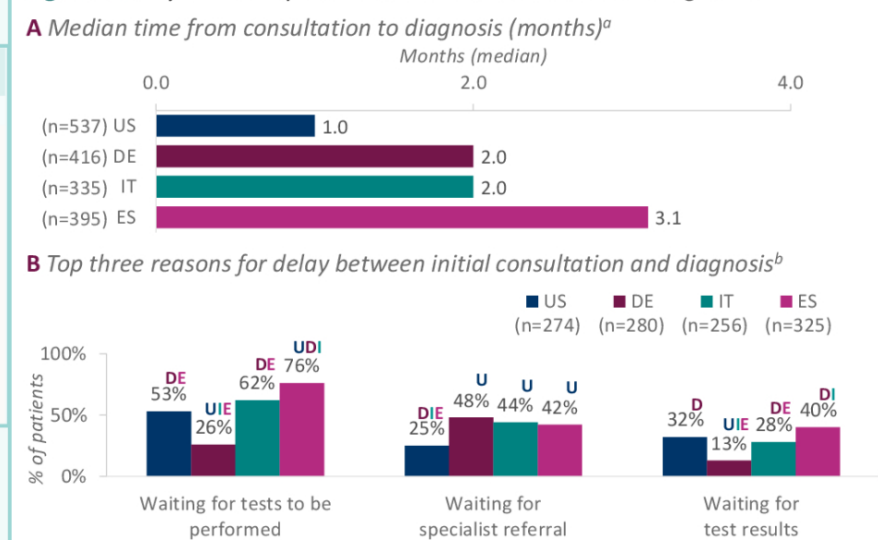
Figure 1. *Patient-reported symptom onset to initial consultation*

A *Mean time from symptom onset to initial consultation (months)*

B *Top three reasons for delay from symptom onset to initial consultation*

Patients with known data. US, United States of America; DE, Germany; IT, Italy; ES, Spain; [UDIE]Superscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083).

Consultation to diagnosis

Patients experienced a further delay of 1-3 months from initial consultation to diagnosis (**Figure 2a**), most commonly due to waiting for tests to be performed in the US, Italy and Spain and waiting for specialist referral in Germany (**Figure 2b**).
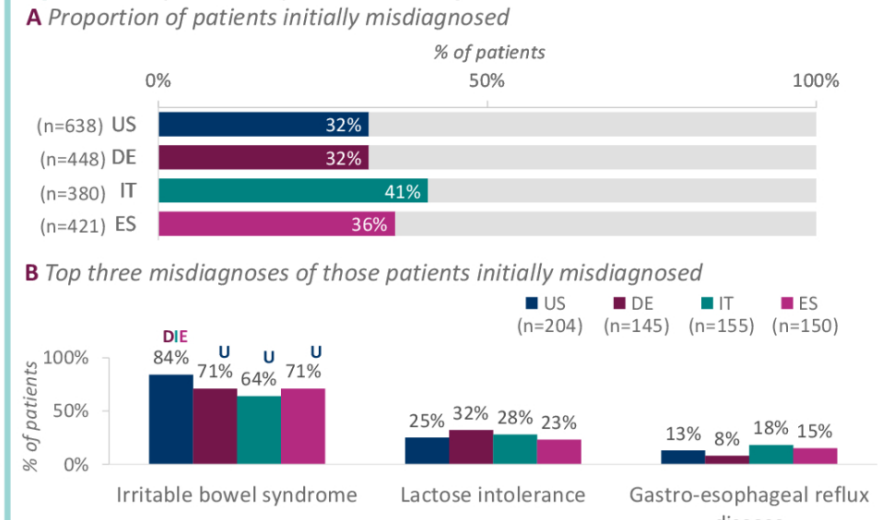
Figure 2. *Physician-reported initial consultation to diagnosis*

A *Median time from consultation to diagnosis (months)[a]*

B *Top three reasons for delay between initial consultation and diagnosis[b]*

[a]Patients with a known diagnosis date; [b]Patients who experienced a delay between consultation and diagnosis. US, United States of America; DE, Germany; IT, Italy; ES, Spain; [UDIE]Superscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083).

Over a third of patients were initially misdiagnosed, significantly higher in Italy compared to the US; the most common misdiagnosis was irritable bowel syndrome, significantly higher in the US compared to the other countries (**Figure 3**).

Figure 3. *Physician-reported misdiagnosis*

A *Proportion of patients initially misdiagnosed*

B *Top three misdiagnoses of those patients initially misdiagnosed*

Patients with known data. US, United States of America; DE, Germany; IT, Italy; ES, Spain; [UDIE]Superscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083).

Diagnosis

Circumstances leading to diagnosis varied across countries: symptom presentation was the most prevalent overall. CeD screening program was higher in Italy compared to all other countries (**Figure 4**).

Figure 4. *Physician-reported events leading to diagnosis*
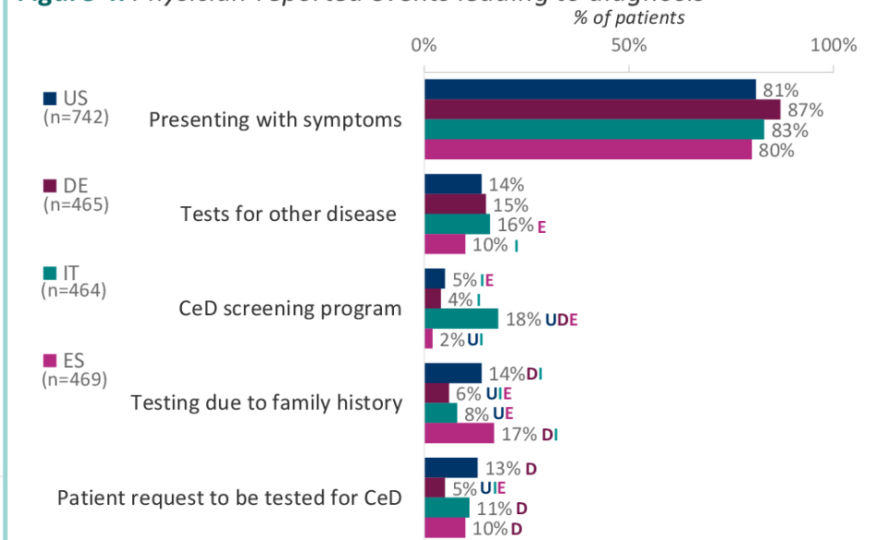
Patients with known data. US, United States of America; DE, Germany; IT, Italy; ES, Spain; CeD, celiac disease; [UDIE]Superscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083).

Patient request to be tested was lowest in Germany, likely due to the low patient awareness of CeD prior to diagnosis (Table 2).

Table 2. *Patient-reported awareness of CeD prior to diagnosis*

	US	DE	IT	ES
n	**287**	**263**	**133**	**251**
Patients aware of CeD prior to diagnosis, n (%)	136 (47.4)[D]	36 (13.7)[IEU]	75 (56.4)[D]	140 (55.8)[D]

CeD, celiac disease; US, United States of America; DE, Germany, IT, Italy; ES, Spain; [UDIE]Superscript letters indicate pairwise significant differences between columns with Bonferroni corrections (p<0.0083).

All diagnostic tests were used significantly less in the US compared to all other countries (Figure 5).

Figure 5. *Physician-reported tests used to diagnose*
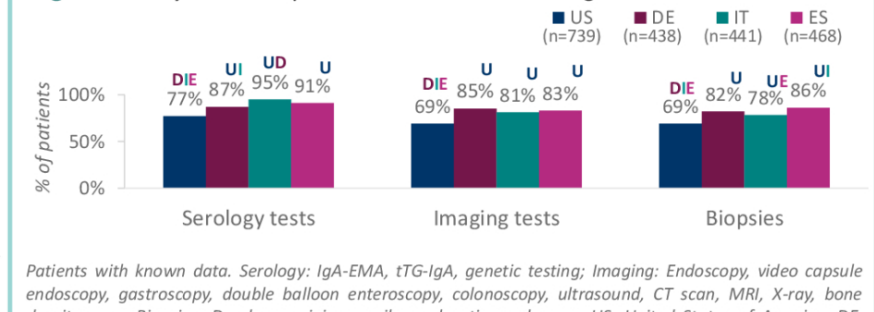
Patients with known data. Serology: IgA-EMA, tTG-IgA, genetic testing; Imaging: Endoscopy, video capsule endoscopy, gastroscopy, double balloon enteroscopy, colonoscopy, ultrasound, CT scan, MRI, X-ray, bone density scan; Biopsies: Duodenum, jejunum, ileum, location unknown; US, United States of America; DE, Germany, IT, Italy; ES, Spain; [UDIE]Superscript letters indicate pairwise significant differences between countries with Bonferroni corrections (p<0.0083).

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