



HAL
open science

Quality of Sleep in Patients with Celiac Disease

Fabiana Zingone, Monica Siniscalchi, Pietro Capone, Raffaella Tortora, Paolo Andreozzi, Elisa Capone, Carolina Ciacci

► **To cite this version:**

Fabiana Zingone, Monica Siniscalchi, Pietro Capone, Raffaella Tortora, Paolo Andreozzi, et al.. Quality of Sleep in Patients with Celiac Disease. *Alimentary Pharmacology and Therapeutics*, 2010, 32 (8), pp.1031. 10.1111/j.1365-2036.2010.04432.x . hal-00566325

HAL Id: hal-00566325

<https://hal.science/hal-00566325>

Submitted on 16 Feb 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Quality of Sleep in Patients with Celiac Disease

Journal:	<i>Alimentary Pharmacology & Therapeutics</i>
Manuscript ID:	APT-0473-2010.R1
Wiley - Manuscript type:	Original Scientific Paper
Date Submitted by the Author:	22-Jul-2010
Complete List of Authors:	Zingone, Fabiana; Federico II University, Department of Clinical and Experimental Medicine Siniscalchi, Monica; Federico II University, Department of Clinical and Experimental Medicine Capone, Pietro; Federico II University, Department of Clinical and Experimental Medicine Tortora, Raffaella; Federico II University, Department of Clinical and Experimental Medicine Andreozzi, Paolo; Federico II University, Department of Clinical and Experimental Medicine Capone, Elisa; Second University of Naples Ciacci, Carolina; Federico II University, Department of Clinical and Experimental Medicine
Keywords:	Coeliac disease < Disease-based, Small intestine < Organ-based, Psychiatric disorders < Topics, Symptom score or index < Topics

1
2
3
4
5
6 1 **Quality of Sleep in Patients with Celiac Disease**

7
8 2 Fabiana Zingone, Monica Siniscalchi, Pietro Capone, Raffaella Tortora, Paolo Andreozzi,

9
10 3 Elisa Capone*, Carolina Ciacci

11
12 4 Department of Clinical and Experimental Medicine Federico II University of Naples, Italy

13
14
15 5 *Second University of Naples, Italy

16
17
18
19
20
21
22
23
24
25
26
27 10
28
29 11
30
31
32 12 **Address for correspondence:**

33
34 13 Dr Carolina Ciacci, MD

35
36 14 Gastroenterology

37
38 15 Dep. Clinical and Experimental Medicine

39
40 16 Via Sergio Pansini, 5 80131 Naples ITALY

41
42 17 tel/fax: +39081746 4270 e-mail: ciacci@unina.it

43
44
45
46 18
47
48 19
49
50 20 **Key words:** sleep quality, quality of life, celiac disease

51
52
53 21
54
55 22 **Short title:** sleep and celiac disease

1

2 **ABSTRACT**

3 **Background:** Celiac disease (CD) is a chronic disease with a various clinical presentation,
4 including anxiety and depression.

5 **Aim:** This study investigated the quality of sleep in CD.

6 **Methods:** The participants were celiacs at diagnosis (C-N); celiacs on gluten free diet at
7 follow-up (C-T); and healthy volunteers (HV). Participants completed the Pittsburgh Sleep
8 Quality Index (PSQI), SF36, Zung and Fatigue scales, and State-Trait Anxiety Inventory
9 (STAI).

10 **Results:** The PSQI score was higher in C-N and C-T than in HV ($p<0.001$). A gluten-free
11 diet (GFD) did not improve the PSQI scores ($p=0.245$) in CD. The other test scores were
12 similar between celiacs at diagnosis and those on a GFD, while significant differences were
13 found between celiacs and volunteers. PSQI score was inversely associated with the quality
14 of the physical ($r=-0.327$, $p=0.002$) and mental ($r=-0.455$, $p<0.001$) components scores.
15 The sleep quality scores were related to depression ($r=0.633$, $p<0.001$), fatigue ($r=0.377$,
16 $p<0.001$), state anxiety ($r=0.484$, $p<0.001$), and trait anxiety ($r=0.467$, $p<0.001$).

17 **Conclusions:** Sleep disorders are common in CD also during treatment with GFD. Sleep
18 disorders are related to depression, anxiety and fatigue, and inversely related to quality of
19 life scale scores.

20

21

22

1 INTRODUCTION

2 In the general population, increased stress, anxiety, depression and worry are associated
3 with poor subjective sleep quality (1). In addition, common medical problems are often
4 associated with abnormalities of sleep. In fact, patients with chronic medical disorders
5 often have fewer hours of sleep and less restorative sleep, as compared to healthy
6 individuals, and this poor sleep may worsen the subjective symptoms of the disorder (2).
7 Among gastrointestinal diseases, gastroesophageal reflux is a major cause of disrupted
8 sleep due to awakenings from heartburn, dyspepsia, coughing, or choking (3). Other
9 gastrointestinal diseases have not been studied.

10 Celiac disease is a chronic disease presenting with a broad spectrum of symptoms
11 and signs. Anxiety, depression, and other mood disorders are associated with celiac disease
12 (4-7). More recently, restless legs syndrome has been shown to be frequent in celiac disease
13 (8). Most of the above-mentioned conditions may affect sleep. As the quality of sleep in
14 celiac disease has not been investigated systematically, this study investigated the quality of
15 sleep in a cohort of adult celiac patients.

17 MATERIALS AND METHODS

18 The study population consisted of adult celiacs consecutively recruited from September
19 2009 to March 2010 from the Celiac Disease Centre of Federico II University (Naples,
20 Italy) and sex- and age-matched volunteers recruited from the hospital staff and friends of
21 CD patients. The study was approved by the Ethical Committee of the Federico II
22 University of Naples (Diagnosis and Follow-up of Celiac Disease n10/2003-2013).

1 The celiacs were divided into two groups: celiac patients at diagnosis on gluten-containing
2 diet (**celiac-new, C-N**) and celiac patients at follow-up **on gluten free diet, since at least one**
3 year and with negative anti-transglutaminase IgA antibody (**celiac-treated, C-T**).

4 **Questionnaires were administered in the morning of the annual visit which is required after**
5 **CD diagnosis for coverage the costs of gluten free food by the Italian National Health**
6 **System. None of patients refused to answer to this questionnaire.** For all celiac patients, the
7 diagnosis was based on the presence of anti-transglutaminase IgA and anti-endomysium
8 antibodies and an intestinal biopsy compatible with gluten-related damage. The control
9 group (**healthy volunteer, HV**) consisted of individuals who were tested and found negative
10 for serum markers of celiac disease.

11 Data were collected on age, gender, marital status, education and **laboratory nutritional**
12 **indices.** The inclusion criteria of the study cohort were written informed consent, age 19 to
13 60 years, absence of major psychiatric disease, absence of cancer, and no pregnancy or
14 children below 3 years old that may affect the quality and modality of sleep.

16 **Pittsburgh Sleep Quality Index**

17 All participants completed the Pittsburgh Sleep Quality Index (PSQI) to evaluate
18 sleep quality. The PSQI was developed to measure sleep quality during the previous month
19 and to discriminate between good and poor sleepers. Sleep quality is a complex
20 phenomenon that involves several dimensions, each of which is covered by the PSQI. The
21 domains covered include subjective sleep quality, sleep latency, sleep duration, habitual
22 sleep efficiency, sleep disturbances, the use of sleep medications, and daytime dysfunction.

1 The PSQI consists of 19 self-rated questions and five questions rated by a bed partner or
2 roommate (only the self-rated items are used in scoring the scale). The self-administered
3 portion consists of 15 multiple-choice items that inquire about the frequency of sleep
4 disturbances and subjective sleep quality, and four write-in items that inquire about typical
5 bedtime, wake-up time, sleep latency and sleep duration. The PSQI generates seven scores
6 that correspond to the domains listed previously. Each component score ranges from 0 (no
7 difficulty) to 3 (severe difficulty). The component scores are summed to produce a global
8 score (range 0–21). A PSQI global score >5 is suggestive of significant sleep disturbance
9 (9,10).

10 To evaluate possible factors contributing to sleep quality, the SF-36 questionnaire,
11 Zung Self-rating Depression Scale, State-Trait Anxiety Inventory and a Fatigue visual
12 analogue scale (VAS), were administered.

13 **SF-36 questionnaire**

14 The SF-36 survey consists of a 36-item questionnaire that includes eight components:
15 physical functioning, role limitations due to physical health, bodily pain, general health,
16 vitality, social functioning, role limitations due to emotional health, and mental health.
17 These eight domains form two broader health dimension scales: the physical (PCS) and
18 mental (MCS) component scales. The SF-36 subscales and composite scores are presented
19 as means and standard deviations and range from 0 to 100, with higher scores indicating
20 better health and well-being. The PCS and MCS composite means and standard deviations
21 are 50 ± 10 for the U.S. general population. PCS and MCS factors have been found to
22 account for 80~85% of the reliable variance in the eight SF-36 scales in patients, as well as

1 in general populations (11-13). Poor (low) scores on the PCS indicate limitations in physi-
2 cal/role functions and general health, and bodily pain, while better (higher) scores suggest
3 no physical limitations, disabilities, or decrements in well-being. Similarly, low scores on
4 the MCS suggest frequent limitations in psychosocial health, emotional problems, and
5 reduced vitality (a fatigue construct), while high scores indicate frequent positive affect and
6 vitality, the absence of psychological distress, and reduced or no limitations in daily social
7 and role activities.

8 **ZUNG Self-rating Depression Scale**

9 The Zung Self-rating Depression Scale is a 20-item self-report questionnaire that is widely
10 used as a screening tool, covering affective, psychological, and somatic symptoms
11 associated with depression (14,15). In this study, depressive symptoms were assessed by a
12 modified version of the Zung Self-rating Depression Scale (M-SDS), which contains 17/20
13 items belonging to the original version of the Zung scale (5,7,16). Three items for
14 gastroenterological symptoms of depression (decreased appetite, weight loss, and
15 constipation) were eliminated to avoid the possible bias due to CD. The cut-off score of the
16 M-SDS scale, for pathological depression is 44.

17 **Fatigue visual analogue scale**

18 This consisted of a single question: 'How did you feel during last week?' The patients were
19 asked to mark a visual analogue scale (VAS) consisting of a 10-cm line with 'I never feel
20 tired' at the left end and 'I always feel tired' at the opposite end. Therefore, the possible
21 score ranges from 0 to 10 (5).

1 State-Trait Anxiety Inventory

2 Anxiety was assessed using the State-Trait Anxiety Inventory (STAI), which consists of
3 two axes (y1 for state anxiety and y2 for trait anxiety), both consisting of 20 multiple-
4 choice items; the STAI can distinguish between existing anxiety and a predisposition to
5 anxious reactions as a personality characteristic, as previously described (17). This theory is
6 based on the conceptual distinction between anxiety as a transitory state and anxiety as a
7 relatively stable personality trait. State anxiety is conceptualised as an emotive state
8 characterised by subjective feelings perceived on a conscious level, such as apprehension
9 and tension, which varies with time; anxiety as a trait refers to individuals with an on-going
10 disposition towards anxiety (18). The subjects evaluated were grouped as high- and low-
11 anxious and a value of 40 was used to distinguish between the two groups, according to
12 Spielberg *et al.* (19) and Weinstein (20).

14 STATISTICAL ANALYSIS

15 Chi-square analysis and ANOVA were used for analyses on categorical and continuous
16 data, respectively. Continuous data were reported as means \pm standard deviation (SD).
17 Categorical data were given as counts and percentages. The Spearman correlation
18 coefficient was used to test for correlations between sleep quality and quality of life scores,
19 depression scale, fatigue severity, STAI scores, and age. The Statistical Package for Social
20 Sciences (SPSS) 13.0 was used to analyze the data. A *p value* ≤ 0.05 was considered
21 significant.

1 RESULTS

2 The study cohort consisted of three groups of 30 subjects each (10 males, 20 females). The
3 age at time of testing, education and marital status were similar among the three groups
4 (Table 1). The patients in C-T had been on a gluten-free diet for 6 ± 5.9 years.

5 Nutritional indices were significantly different in C-N and C-T (blood hemoglobin:
6 11.67 ± 0.87 g/dL and 12.3 ± 0.52 g/dL respectively, $p=0.002$; plasma cholesterol:
7 165.6 ± 13.47 mg/dL and 191.46 ± 21.73 mg/dL respectively, $p < 0.001$; serum albumin:
8 3.67 ± 0.88 mg/dL and 4.09 ± 0.37 mg/dL respectively, $p < 0.001$; body mass index:
9 21.6 ± 2.55 Kg/m² and 24.8 ± 3.43 Kg/m² respectively, $p= 0.007$).

11 PSQI results

12 A progressive decrease of the score indicating pathological sleep, was found among
13 the three groups ($p < 0.001$). The comparison between the two celiac groups indicated that
14 the PSQI score, did not differ between C-N and C-T ($p > 0.2$) (Table 2).

15 The analysis of the single domains of the PSQI (subjective sleep quality, sleep
16 latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep
17 medications, and daytime dysfunction) indicated a significant difference between celiac
18 patients (both C-N and C-T) and volunteers for each domain ($p < 0.05$), except for sleep
19 duration, which was similar in the three groups ($p = 0.166$).

20 SF36 results

21 The comparison of each single domain of the SF36 and the PCS and MCS values did not
22 show differences between celiacs at diagnosis and celiac on a gluten-free diet. The quality

1 of life of CD patients, (C-N and C-T) was significantly lower than that of the volunteers for
2 each domain (Figure 1).

3 **Zung, fatigue, and anxiety scale results**

4 Celiac patients showed a significant difference in the modified Zung scale scores, fatigue
5 VAS scores, and STAI y1 and y2 scale scores, as compared to volunteers. The results did
6 not significantly differ between untreated celiacs and celiacs on gluten free diet (Table 3).

7 Only two persons from C-N and two from C-T had a modified Zung score above the
8 threshold for major depression. Findings were similar after the exclusion of these patients
9 (C-N 5.92 ± 3.52 ; C-T 4.82 ± 2.14 ; HV 2.96 ± 2.86 ; $p = 0.001$).

10 Nineteen persons from C-N, 16 from C-T, and 13 from HV scored above 40, for
11 STAI-y1 ($p = 0.3$), scores more than 40 indicate an anxiety state; 17 persons from C-N, 15
12 from C-T, and 8 from HV scored above 40 for STAI-y2 ($p = 0.05$), scores more than 40
13 indicate an anxiety trait.

14 The PSQI score of all participants was inversely associated with the quality of the
15 physical ($r = -0.327$, $p = 0.002$) and mental ($r = -0.455$, $p < 0.001$) component scores, while
16 there were significant positive correlations between sleep quality and depression (Zung
17 $r = 0.633$, $p < 0.001$), fatigue ($r = 0.377$, $p < 0.001$), state anxiety ($r = 0.484$, $p < 0.001$), and trait
18 anxiety ($r = 0.467$, $p < 0.001$).

19 The age at testing was not related to sleep quality ($r = 0.105$, $p = 0.323$). In addition,
20 gender ($p = 0.295$), education ($p = 0.307$), marital status ($p = 0.223$), and gastrointestinal
21 symptoms ($p = 0.403$) were not related to sleep quality.

1 DISCUSSION

2 Data from this study indicated that sleep disorders are common in untreated celiac disease
3 and should be considered a symptom of the disease. Sleep does not improve with a gluten-
4 free diet, although the score tended to decrease, but did not reach those of the non-celiac
5 **volunteers**. In detail, in celiac patients, all items explored by the PSQI but one —sleep
6 duration— are impaired in comparison with **volunteers**. In celiac patients, sleep disorders
7 are directly related to depression, anxiety, and fatigue and inversely related to quality-of-
8 life scale scores. Age, gender, education, marital status, and the presence of gastrointestinal
9 symptoms do not relate to the presence of sleep disorders.

10 Analysis of the SF36 questionnaire indicated that the scores on the PCS were low
11 before starting a gluten-free diet, indicating limitations in physical/role functions, bodily
12 pain, and general health, and these did not improve after treatment. The MCS score tended
13 to decrease on a gluten-free diet. As a low MCS score suggests frequent limitations in
14 psychosocial health, emotional problems, and reduced vitality (a fatigue construct), the data
15 suggest that living with the limitations imposed by a gluten-free diet induces a worsening
16 of psychosocial health and generates limitations in daily social and role activities.

17 This finding suggests that the sleep disorders are not related to the presence of
18 gastrointestinal symptoms at diagnosis, and is why they did not improve on the diet, in
19 contrast with the disappearance or improvement of most of the other symptoms.

20 The evaluation of the depression and anxiety scales scores in celiacs indicates that
21 celiacs are more anxious and depressed than **volunteers**. In celiacs, however, a gluten-free
22 diet did not induce any significant improvement in the score for any scale. This is in

1 contrast with the study of Addolorato, which found a significant improvement in state
2 anxiety, but not depression, after one year of a gluten-free diet. One possible explanation is
3 that celiacs from Addolorato study were evaluated after one year of gluten free diet. Our
4 celiacs have been evaluated after an average of six years from diagnosis. This different time
5 lapse might have played a role for the persistence (or renewal) of anxiety in our celiacs on
6 gluten free diet.

7 The present study has the limit of a comparison with general population controls. On the
8 other hand, a comparison with other chronic diseases is anyway unfeasible for the peculiar
9 characteristics of celiac disease, the limitations imposed by gluten free diet and the
10 disappearance of symptoms after some time from the beginning of the diet. However, the
11 study was designed to reduce the effect of this limitation. The PSQI was administered at
12 time of the first visit, hence when the person referring to the CD center had not yet received
13 any previous CD diagnosis. The selection of any other GI disease as control group would
14 have raised the problem of comparability because common GI diseases most often are with
15 a clinical presentation and a 'disease status' heavier than CD.
16 Finally, the metabolic status of the treated group was much better than one of the untreated
17 group. Thus, the data indicate at least that sleep disorders in celiac disease are not fully
18 controlled after six-years of gluten-free diet despite of a substantial improvement of the
19 metabolic status.

20 In conclusion, our study confirms previous observations of a poor quality of life in
21 celiacs both before and after diet treatment. For the first time, our findings indicate that
22 sleep disorders are a frequent complaint in celiacs and should be added to the wide

- 1 spectrum of symptoms and signs of CD. Studies should determine if medical therapy that
- 2 improves sleep also improves the quality of life of celiac patients on a gluten-free diet.
- 3 Longitudinal studies are needed to confirm the present findings and to assess the effect of
- 4 gluten free diet .

For Peer Review

REFERENCES

1. Specchio LM, Prudeniano MP, de Tommaso M, et al. Insomnia, quality of life and psychopathological features. *Brain Res Bull.* 2004 Jun 30;63(5):385-91.
2. James M. Parish. Sleep related problems in common medical conditions. *Chest.* 2009 Feb;135 (2):563-570
3. Kahrilas PJ. Obstructive sleep apnea and reflux disease: bedfellows at best. *Chest.* 2010 Apr;137(4):747-8
4. Addolorato G, Mirijello A, D'Angelo C, et al. State and trait anxiety and depression in patients affected by gastrointestinal diseases: psychometric evaluation of 1641 patients referred to an internal medicine outpatient setting. *Int J Clin Pract.* 2008 Jul;62(7):1063-9. Epub 2008 Apr 18.
5. Siniscalchi M, Iovino P, Tortora R, et al. Fatigue in adult coeliac disease. *Aliment Pharmacol Ther.* 2005 Sep 1;22(5):489-94
6. Ludvigsson JF, Reutfors J, Osby U, Ekbohm A, Montgomery SM. Coeliac disease and risk of mood disorders-A general population-based cohort study. *J Affect Disord.* 2007 Apr;99(1-3):117-26. Epub 2006 Oct 6.
7. Addolorato G, Capristo E, Ghittoni G, et al. Anxiety but not depression decreases in coeliac patients after one-year gluten-free diet: a longitudinal study. *Scand J*

- 1
2
3
4
5
6 Gastroenterol. 2001 May;36(5):502-6.
7
8
9
10 8. Moccia M, Pellicchia MT, Erro R., et al. Restless legs syndrome is a common
11 feature of adult celiac disease Movement Disorders - April 13, 2010
12
13
14 9. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh
15 Sleep Quality Index: A new instrument for psychiatric practice and research.
16 Psychiatry Res 1989;28:193-213
17
18
19
20 10. Buysse DJ, Reynolds CF, Monk TH, et al. Quantification of subjective sleep
21 quality in healthy elderly men and women using the Pittsburgh Sleep Quality
22 Index. Sleep 14:331-338, 1989b
23
24
25
26
27
28 11. Ware JE, Kosinski M, Keller SD. SF-36 physical and mental health summary
29 scales: A user's manual. Boston, MA: The Health Institute, New England
30 Medical Center, 1994.
31
32
33
34
35
36 12. Ware JE. SF-36 health survey update. Spine 2000;25:3130-9.
37
38
39 13. Ware JE Jr, Kosinski M, Bjorner JB, Turner Bowker-DM, Gandek B, ME
40 Maruish. User's manual for the SF-36v2 health survey (2nd ed.). Lincoln, RI:
41 Quality Metric Incorporated, 2007.
42
43
44
45 14. Hadjivassiliou M, Gibson A, Davies-Jones GAB, Lobo AJ, Stephenson TJ,
46 Milford-Ward A. Does cryptic gluten sensitivity play a part in neurological
47 illness? Lancet 1996; 347: 369-71.
48
49
50
51
52 15. Zung W. From art to science. Arch Gen Psychiatry 1973; 29:328-37.
53
54
55
56
57
58
59
60

- 1
2
3
4
5
6
7 16. Ciacci C, Iavarone A, Mazzacca G, De Rosa A. Depressive symptoms in adult
8
9 celiac disease. Scand J Gastroenterol. 1998 Mar;33(3):247-50.
10
11
12 17. Peterson R.A. and Reiss R.L. (1987). The anxiety sensitivity index: Construct
13
14 validity and factor anal analytic structure. Journal of Anxiety Disorders. (1), 265-
15
16 277.
17
18 18. Spielberger C. D., Gorsuch R.L., and Lushene. R.E. (1970). Manual for the
19
20 State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press
21
22
23 19. Spielberger C. D., Reheiser E.C., Ritterband L.M., Sydeman, S.J., and Unger,
24
25 K.K. Assessment of Emotional States and Personality Traits: Measuring
26
27 Psychological Vital Signs. In Butcher, J.N. (Ed.) Clinical Personality
28
29 Assessment: Practical Approaches. New York: Oxford University Press, 1995.
30
31
32 20. Weinstein AM. Visual ERPs evidence for enhanced processing of threatening
33
34 information in anxious university students. Biol Psychiatry. 1995 Jun
35
36 15;37(12):847-58.
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8

1 **Table 1.** Demographics of the study population (celiac-new C-N, celiac-treated C-T,
 2 healthy volunteer HV)

	C-N	C-T	HV	<i>p</i>
Number of patients	30	30	30	1.000
Women/Men	20/10	20/10	20/10	1.000
Age at testing (years)	33.10±11.46	36.20±11.53	34±11.61	0.586
Education: high school or less/beyond high school	20/10	25/5	21/9	0.303
Married/Partnered (%)	56.66	63.33	53.33	0.956

3

1 **Table 2.** The percentage of scores indicating pathological sleep and the mean±SD of the
2 PSQI results for celiac patients at diagnosis (celiac-new, C-N), on a gluten-free diet (celiac-
3 treated, C-T), and volunteer (healthy volunteer, HV).

	C-N	C-T	HV	<i>p</i>
%PSQI pathological (>5)	50%	33.3%	23.33%	0.093
PSQI in the three groups	6.20±3.64	5.23±2.64	2.96±2.86	<0.001

4

Table 3. The mean±SD of the scores of the modified Zung scale for depression, the VAS (1 to 10) for fatigue, and STAI-y1 and -y2 for state and trait anxiety in the study population (celiac-new C-N, celiac-treated C-T, healthy volunteer HV)

	C-N	C-T	HV	<i>p</i>
Modified Zung	34.23±6.73	31.40±7.19	25.40±5.85	<0.001
Fatigue VAS	6.13±2.54	5.5±2.17	3.43±2.36	<0.001
STAI-y1	46.23±10.70	43.90±10.95	37.70±8.67	0.005
STAI-y2	42.90±8.10	42.73±9.55	36.23±8.02	0.004

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 1. The mean±SD of the eight component scores of the SF36 questionnaire (physical functioning, role limitations due to physical health, bodily pain, general health, vitality, social functioning, role limitations due to emotional health, and mental health) and the mean±SD of the physical (PCS) and mental (MCS) component scales in celiac patients at diagnosis (**celiac-new, C-N**), on a gluten-free diet (**celiac-treated, C-T**), and **volunteers (healthy volunteer, HV)**.

For Peer Review

1

2 **Acknowledgements:** The work of Monica Siniscalchi, Psichol. Dr. was supported by a

3 Regione Campania grant

4

5

6 **Conflict of interest to declare:** none

7

8

9

10

11

12 The English in this document has been checked by at least two professional editors, both

13 native speakers of English. For a certificate, please see:

14 <http://www.textcheck.com/certificate/Wcg1AX>

15

16

17

18

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

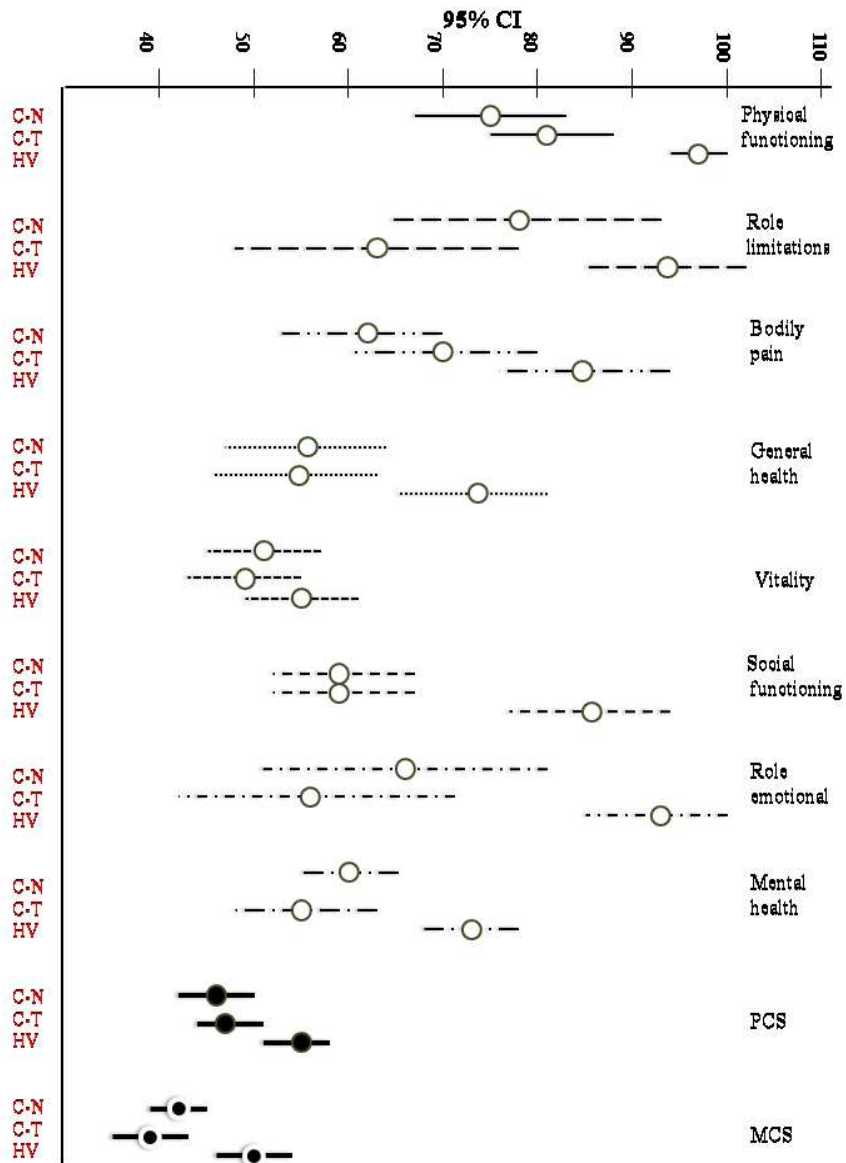


Figure 1
190x254mm (96 x 96 DPI)