Title: Reduced quality of life in coeliac disease is more strongly associated with depression than gastrointestinal symptoms

Short title: Quality of life in coeliac disease

Key words: Coeliac disease, quality of life, gluten free diet adherence, depression

Authors: Kirby Sainsbury, B Ed/BA (Psychology Honours), Doctor of Clinical Psychology/PhD candidate (under examination) [a]

Barbara Mullan, PhD [b]

Louise Sharpe, PhD [a]

[a] Clinical Psychology Unit, the University of Sydney

[b] School of Psychology, the University of Sydney

Corresponding author: Barbara Mullan

Address: School of Psychology, the University of Sydney, NSW, 2006, AUSTRALIA

Email barbara.mullan@sydney.edu.au Phone: + 61 2 9351 6811 Fax: + 61 2 9036 5223

Financial support: None

Conflicts of interest: None

Acknowledgements: The Coeliac Society of NSW, Australia; Health Psychology Lab Group, the University of Sydney

Word count: 4287

ABSTRACT

Objective: Despite evidence indicating a heightened incidence of psychological symptoms in coeliac disease (CD), the direct link between psychological factors and quality of life (QOL) has received little attention. The purpose of this paper was to compare the relative impacts of psychological symptoms and coping to the known negative impacts of gastrointestinal symptoms and adherence to the gluten free diet (GFD) on QOL.

Methods: In study 1 (N = 390), participants completed measures of QOL, psychological symptoms, coping, several indices of symptom severity, and adherence. Correlations and regression analyses were used to determine the relationships between QOL and the measured variables. Study 2 (N = 189) replicated the findings using a validated measure of current gastrointestinal symptom severity and more a comprehensive measure of coping.

Results: Across both studies, poorer QOL was correlated with a higher incidence of psychological and gastrointestinal symptoms, greater reliance on maladaptive coping strategies, and poorer GFD adherence. The relationship between psychological symptoms (particularly depression) and QOL persisted when controlling for past (study 1) and current (study 2) gastrointestinal symptom severity. Psychological symptoms and GFD adherence were more strongly related to reduced QOL than gastrointestinal symptoms.

Conclusion: The negative impact of psychological symptoms on QOL and adherence suggests that management in CD should include the provision of psychological coping skills, as well as purely dietetic-based strategies to minimise gastrointestinal symptoms.

Coeliac disease (CD) is a chronic autoimmune disorder involving intolerance for dietary gluten (1). Consequently, treatment involves the removal of all gluten from the diet, and indeed the only available treatment is strict adherence to a lifelong gluten free diet (GFD) (1, 2). The clinical presentation of undiagnosed or untreated CD can include symptoms relating to the malabsorption of nutrients (e.g., iron/calcium deficiencies, fatigue, weight loss), as well as gastrointestinal symptoms resulting from damage to the small intestine (e.g., diarrhoea, cramping) (3, 4). The disease can manifest as classical (diarrhoea either with or without accompanying malabsorption symptoms), atypical (gastrointestinal symptoms are absent/not prominent; extra-intestinal symptoms often prompt diagnosis), or silent (no symptoms present) (4). If left untreated or poorly managed, CD has been linked to several long-term health complications including intestinal and bowel cancers, osteoporosis, and infertility (5).

CD is a genetically mediated condition (6), and is estimated to affect approximately 1% of the population, making it the most prevalent autoimmune disorder in the world (7, 8). Serological prevalence rates do, however, differ between countries; for example, a recent international screening study found rates of 2.4% in Finland, while only 0.3% in Germany (9). Due to the varied presentation of CD it is estimated that up to 75% of cases remain undiagnosed (2, 10, 11). CD can develop at any age, although peaks in diagnosis have been observed in early childhood and the fourth and sixth-to-seventh decades of life (12). Consistent with most autoimmune disorders, CD is more common in females than males (ratio of 2-3:1), although the reason for this is not known (3, 7).

Reduced quality of life (QOL) has been commonly observed in patients with CD compared to healthy control participants (13-18). Investigations have focused largely on demographic (e.g., gender, whereby females commonly report poorer QOL than males) (15, 19-

21); medical (e.g., gastrointestinal symptoms, whereby more severe symptoms are associated with poorer QOL) (22-27); and dietary (e.g., GFD adherence, whereby poorer adherence is associated with poorer QOL; and perceived difficulty of adherence, which was also associated with poorer QOL) (23, 28-30) aspects of the disease. While these factors are important for QOL, one area that has received less attention is psychological symptoms and coping, despite higher rates of psychological symptoms within CD patients compared to the general population (16, 31-36). Two studies found that increased depression and anxiety in CD were correlated with reduced QOL (16, 36), while a recent study found that emotion-oriented coping was negatively related to QOL (37). In the broader context, the link between QOL, psychopathology, and coping is well established (38-42), with depression representing the greatest threat to QOL across a range of populations (38). Together these findings suggest that psychological symptoms and coping are likely to be highly relevant to QOL in CD and warrant further attention.

Further, research in a range of medical conditions has also demonstrated a direct link between the severity of gastrointestinal and psychological symptoms (43). For example, Walker and colleagues (44) found that patients suffering from inflammatory bowel disease with depression reported more severe gastrointestinal symptoms than those without depression. It was suggested that the presence of a psychological condition such as depression might serve to exacerbate the perception of physical symptoms (43, 44), both of which would then likely have a negative impact on QOL. Similarly, it was found that the majority of patients suffering from gastrointestinal disorders (including CD) presenting for treatment also showed symptoms of depression or elevated state anxiety (45).

In CD, investigations into gastrointestinal and psychological symptoms and their relation to QOL have largely been conducted in isolation. In one study, Hauser and colleagues (24)

examined the impact of gastrointestinal symptoms and probable mental disorder (measured by a self-report questionnaire) on physical and psychological QOL and found that gastrointestinal symptoms but not psychological symptoms had a significant negative impact on physical QOL. The opposite pattern of results was observed for psychological QOL (24). This finding is not surprising given the degree of overlap between items designed to assess physical QOL and symptom severity, and psychological symptoms and psychological QOL. An important question that remains unanswered, however, is how gastrointestinal and psychological symptoms jointly impact QOL.

The studies reported here therefore had two aims: (1) to determine the relative magnitude of the impact of psychological symptoms and coping on QOL in CD compared to the known negative impacts of female gender, inadequate GFD adherence, and increased gastrointestinal symptom severity; and (2) to examine the nature of the relationship between psychological symptoms and gastrointestinal symptom severity, and their joint impact on QOL. In the first study it was hypothesised that:

- Poorer QOL would be associated with a higher incidence of psychological symptoms and increased reliance on maladaptive coping strategies, as well as poorer GFD adherence, female gender, and increased gastrointestinal symptom severity;
- A relationship between gastrointestinal symptoms and psychological symptoms would exist, whereby individuals reporting more severe gastrointestinal symptoms would also exhibit more symptomatic psychological profiles;
- Psychological symptoms would be more strongly associated with QOL than gastrointestinal symptoms;

- The negative impact of psychological symptoms on QOL would persist after controlling for gastrointestinal symptom severity.

STUDY 1 METHOD

Participants and procedure

A recruitment email was sent to a randomly selected sample (N = 2989; October, 2010) of members of the Coeliac Society of New South Wales who were identified via a database screen as meeting the following inclusion criteria: biopsy-confirmed CD, GFD duration >3 months, aged >16 years. All data was collected and submitted anonymously online and took approximately 20 minutes. The data used in this study was originally collected with the aim of identifying the factors contributing to the intention-behaviour gap in GFD adherence and has been published elsewhere (46). It was, however, beyond the scope of that paper to also examine QOL.

Measures

Participants completed demographics questions (age; gender; education; marital and employment status), and the following CD variables: age at diagnosis; symptom duration prior to diagnosis; duration of GFD; time to improvement after initiation of the GFD; family history of CD; and additional dietary allergies/intolerances (including dairy, egg, peanut, tree-nuts, shellfish, seafood, soy, and other) and medical comorbidities (free response). Gastrointestinal symptom severity was operationalised in two ways: current symptom severity represented the severity of symptoms when consuming gluten since initiation of the GFD, while consistent with a previous study (18), past symptom severity reflected the number of symptoms from a list of common CD symptoms that were endorsed as having been experienced prior to diagnosis.

QOL was assessed using the overall QOL item ("How would you rate your quality of life?") from the World Health Organisation Quality of Life Assessment (WHOQOL-BREF; 47). Scores range from 1-5, with higher scores indicating better QOL. The decision to use the single item rather than the entire scale to measure QOL was based on the significant and positive correlations observed between overall QOL and each of the domain scores in a previous sample of patients with CD (29). The Depression Anxiety Stress Scale (48, 49) was used to measure the negative emotional states of depression (e.g., "I felt downhearted and blue"), anxiety ("I felt I was close to panic"), and stress ("I tended to overreact to situations"). The scale contains 21 items; subscale scores range from 0-42, and higher scores indicate more severe/frequent symptoms (49). The Eating Disorder Inventory-3 Eating Disorder Risk Scale (50) provided a measure of eating disorder symptomatology. The scale contains 25 items (e.g., "I eat when I am upset" and "I think about dieting"); raw scores range from 0-100, and higher scores indicate more severe eating disorder symptoms. The Coping Inventory for Stressful Situations (51) was used to measure adaptive (task-oriented; e.g., "Focus on the problem and see how I can solve it") and maladaptive (emotion-oriented; e.g., "Blame myself for being too emotional about the situation") coping. The scale contains 21 items measuring three distinct coping strategies (task-oriented, emotion-oriented, and avoidance); however, the avoidance subscale was not included in analyses as it failed to correlate with any of the other variables of interest (46). Scores range from 7–35, with higher scores indicating more frequent use of the coping strategy (51). GFD adherence was measured using the Coeliac Dietary Adherence Test (52), which is a seven-item questionnaire shown to correlate highly with dietitian rated estimates of adherence (the gold standard). It contains items pertaining to three relevant domains: CD-related symptoms (2 items; e.g., "Have you been bothered by low energy levels in the past four weeks?"), self-efficacy (3

items; e.g., "I do not consider myself a failure"), and gluten avoidance habits (2 items; e.g., "How important to your heath are accidental gluten exposures?"). Scores range from 7-35, with higher scores indicating poorer adherence. The perceived difficulty of adhering to the GFD was assessed using the Perceived Behavioural Control scale of the Coeliac Disease Theory of Planned Behaviour Questionnaire (29). The scale contains four items (e.g., "How much personal control do you feel you have over maintaining a strict gluten free diet?"); scores range from 1-7, and higher scores indicate a higher perception of control over managing the GFD.

Statistical analyses

All analyses were conducted using the Statistical Package for the Social Sciences (SPSS 18.0). Correlations and *t*-tests were used to examine the relationships between QOL and the continuous and categorical variables respectively. Based on the CD data collected, several indices indicative of gastrointestinal symptoms were analysed including past and current symptom severity, reason for diagnosis, time to improvement after initiation of the GFD, and additional dietary intolerances and medical comorbidities. A hierarchical regression analysis predicting QOL was conducted, whereby the variables that showed significant relationships with QOL in the univariate analyses were entered as independent variables in three steps: 1) disease characteristics; 2) adherence variables (actual adherence and perceived difficulty); and 3) psychological and coping variables. Gender was controlled for due to gender differences observed on several of the disease and psychological variables. All analyses were two-tailed with a significance level of $\alpha = 0.05$.

STUDY 1 RESULTS

Sample characteristics

Three hundred and ninety individuals completed the survey (response rate = 13%; mean age = 44.2; *SD* = 12.7; 82.8% female). Most participants were either married or living with a partner (76%), and were engaged in full time or part time/casual work (74%), with a small number being unemployed, retired, or students. Overall the sample was well educated, with 74% having completed education beyond year 12. Table 1 shows a summary of the sample characteristics, and the relationships with QOL.

The mean QOL score was comparable to the average Australian population norms (47). The mean scores on each of the psychological symptom measures fell within the normal ranges (49-51). The mean adherence score fell in the excellent or very good range (52.7% excellent or very good; 36.4% moderate; 6.8% fair to poor) (52). The mean score for perceived difficulty indicated predominantly positive perceptions about the ability to manage the GFD (29).

INSERT TABLE 1 HERE

Demographic and disease factors

Poorer QOL was significantly associated with a greater number and longer duration of CD symptoms prior to diagnosis, and a longer time to improvement after initiation of the GFD (see Table 1). Participants who reported suffering from additional dietary intolerances ($M = 4.00$; $SD = 0.87$) had poorer QOL than those who did not ($M = 4.34$; $SD = 0.72$). Screen-detected patients ($M = 4.39$, $SD = 0.72$) had better QOL than symptom-detected patients ($M = 4.21$, $SD = 0.79$), and post-hoc analyses indicated this difference was mediated by the higher number of symptoms reported by the symptom-detected group (symptom-detected: $M = 6.32$, $SD = 2.27$; screen-detected: $M = 4.74$, $SD = 2.59$; $t = 5.79$, $p < .001$; Sobel statistic = 3.42, $p < .001$). There were no gender differences in QOL, although females reported a greater number of symptoms (females: $M = 6.15$, $SD = 2.41$; males: $M = 4.82$, $SD = 2.41$, $t = -4.01$, $p < .001$) and more severe

recurrence of symptoms when consuming gluten since diagnosis than males ($\chi = 12.79$, $p < .05$). Adherence and QOL were significantly related, as were the perceived level of difficulty associated with maintaining a strict GFD and QOL.

Psychological symptoms and coping

Reduced QOL was significantly associated with higher levels of psychological symptoms and greater reliance on maladaptive coping (increased emotion-oriented and decreased task-oriented; see Table 1). More severe gastrointestinal symptoms at diagnosis were also associated with increased depression ($r = 0.18$, $p < .01$), anxiety ($r = 0.29$, $p < .001$), stress ($r = 0.28$, $p < .001$), eating disorder risk ($r = 0.15$, $p < .01$), and emotion-oriented coping ($r = 0.17$, $p < .01$), but not with task-oriented coping ($p > .05$).

Predicting QOL

Gender and the disease characteristics accounted for 13.1% of the variance in QOL, although only the number of symptoms, time to improvement, and additional intolerances made significant independent contributions. Adherence and perceived difficulty added 14.3%, with adherence but not difficulty making an independent contribution. The addition of psychological symptoms and coping at step 3 brought the total variance accounted for to 44.5% (+17%), although only depression had a significant independent effect. The effects of number of symptoms, additional intolerances, time to improvement, and GFD adherence remained significant (see Table 2).

INSERT TABLE 2 HERE

STUDY 1 DISCUSSION

As predicted, reduced QOL was related to heightened levels of psychological symptoms and maladaptive coping, poorer GFD adherence, and past (but not current) gastrointestinal

symptom severity. Longer duration of symptoms, longer time to improvement after initiation of the GFD, and the presence of additional dietary intolerances were also related to poorer QOL. Contrary to predictions, and inconsistent with previous research in CD (15, 19, 21) and across a wide variety of health conditions (53, 54), no gender differences in QOL were observed. Although the uneven gender distribution in this study is consistent with both the gender distribution of CD diagnoses (3) and the gender breakdown of the Coeliac Society's database (55), it is possible that the predominance of females may have obscured potential differences. Alternatively, gender differences in QOL may not be as prevalent in CD sufferers in Australia.

Consistent with the hypotheses, psychological factors and adherence were more strongly related to reduced QOL in individuals with CD than gastrointestinal symptoms. Further, although heightened symptom severity was indeed predictive of poorer QOL, the effect was reduced when GFD adherence and psychological symptoms were included. The relationship between heightened psychological symptoms and more severe gastrointestinal symptoms was also confirmed. This pattern of relationships has been reported in other illness populations (43, 44) but this study is the first to demonstrate such a link in CD. As was suggested by previous researchers (43, 44), it is possible that the presence of psychological symptoms, even at subclinical levels, resulted in the increased salience and subsequent reporting of gastrointestinal symptoms. These results also extend previous findings (24) by demonstrating that in addition to affecting physical and psychological QOL respectively, gastrointestinal and psychological symptoms both have negative impacts, albeit of differing strength, on overall QOL.

The findings regarding coping were consistent with previous research (37), whereby the increased use of emotion-oriented coping was more strongly related to reduced QOL than the decreased use of task-oriented coping. The observation that coping was not predictive of QOL

after controlling for psychological symptoms also parallels previous findings in GFD adherence (46). It may be the case that coping plays a role in the development of psychological symptoms and ability to manage the GFD, as well as the perception of gastrointestinal symptoms, which in turn directly impact QOL. It has been suggested that difficulty in following the GFD rather than actual adherence exerts a negative impact on QOL (28). In contrast, here it was found that actual adherence to the GFD had a far greater negative impact on QOL than did the perceived level of difficulty; supporting the assertion that inadequate adherence does play an important role in QOL for individuals with CD.

A limitation of this study was the reliance on the number of symptoms experienced prior to diagnosis as a proxy measure for gastrointestinal symptom severity. While symptom severity at diagnosis using this type of measure has been linked to reduced QOL (18), *current* symptom severity probably represents a better predictor of QOL, as well as having the advantage of potentially being modifiable for intervention purposes. Here the measure of current symptom severity was specific to symptoms experienced when consuming gluten post GFD onset, and was not related to QOL. There are, however, a proportion of people who experience refractory CD; that is, the persistence of clinical symptoms *despite* being adherent to a strict GFD (56-58). Indeed, a recent study found a strong link between refractory CD and reduced QOL (59), suggesting that current symptom severity generally, rather than specific to gluten consumption, is likely to offer more insight into the relationship between gastrointestinal symptoms and QOL. Additional limitations will be discussed in the context of the general discussion.

STUDY 2 AIMS AND HYPOTHESES

Derived from the limitations of study 1, the primary aim of study 2 was to confirm the differential relationships between gastrointestinal symptoms, QOL, and psychological symptoms

by using a more reliable and well-validated measure of current symptom severity. It was hypothesised that while increased gastrointestinal symptoms, poorer GFD adherence, increased psychological symptoms, and reliance on maladaptive coping would predict reduced QOL, psychological symptoms would be more strongly related to QOL than gastrointestinal symptoms, and that the relationship between psychological symptoms and QOL would persist when controlling for gastrointestinal symptoms.

STUDY 2 METHOD

Participants and procedure

Participants were the baseline sample recruited to an online intervention to improve GFD adherence, coping, and QOL in CD (60). The recruitment strategy (email sent to 1500 members; April 2012), inclusion criteria, most measures, and procedure in this study were identical to study one. A description of the intervention content, procedure, and the trial outcome have been reported elsewhere (60); however, as in study 1 it was beyond the scope of that paper to examine the predictors of reduced QOL. For the purposes of the current analyses the baseline intervention sample was analysed cross-sectionally.

Additional measures and analyses

The Coeliac Disease Questionnaire (CDQ) – Gastrointestinal Symptoms subscale (61) provided a validated measure of current symptom severity, replacing the previous questions regarding the number and severity of symptoms experienced. The gastrointestinal symptoms subscale has seven items; scores range from 0-49, and higher scores indicate fewer/less severe gastrointestinal symptoms.

In addition, the Brief COPE (62) replaced the Coping Inventory of Stressful Situations (51). This decision was based on the observation that coping did not add significantly to the

prediction of QOL (study 1) or GFD adherence (46) once psychological symptoms were included in the model, with the hope that a more comprehensive measure of the coping strategies employed by people with CD rather than the simple division into task-oriented and emotion-oriented coping may further elucidate the role of coping in QOL. The scale contains 28 items measuring 14 distinct coping strategies; subscale scores range from 2-8, and higher scores indicate more frequent use of the coping strategy. Participants were asked to rate each coping strategy specifically according to how frequently they used it in relation to managing the challenges associated with the GFD. The statistical analyses conducted in study one were repeated here.

STUDY 2 RESULTS

Sample characteristics

One hundred and eighty-nine individuals completed the baseline survey (response rate = 12.6%; mean age = 46.5, *SD* = 14.7; 87.3% female). Table 3 shows a summary of the sample characteristics and their relationships to QOL. The mean gastrointestinal symptom score was high indicating low severity of current symptoms (61). Regarding coping, the adaptive strategies (e.g., acceptance, active coping, planning,) were all used more frequently than the maladaptive ones (e.g., self-distraction, denial, self-blame,), and only the maladaptive strategies (plus seeking emotional support) were related to QOL.

INSERT TABLE 3 HERE

Predicting QOL

Gender and current symptom severity accounted for 3.6% of the variance in QOL, although only symptoms made an independent contribution (see Table 4). Adherence and perceived difficulty contributed a further 7.7%, with adherence but not difficulty being

significant, and the effect of symptoms being reduced to non-significance. The addition of psychological symptoms added 23.8% to the model (total = 35.2%), with depression reducing the effects of both gastrointestinal symptoms and adherence to non-significance. Coping did not add to the prediction over and above psychological symptoms ($p > .05$; not shown).

INSERT TABLE 4 HERE

STUDY 2 DISCUSSION

This study confirmed the significant correlations observed in study one between reduced QOL and improved GFD adherence, heightened psychological symptoms and maladaptive coping, and increased gastrointestinal symptom severity, as well as between more severe gastrointestinal and psychological symptoms. Also consistent with study one was the differential magnitude of the relationships, with psychological symptoms again being more strongly related to reduced QOL than gastrointestinal symptom severity or the perceived difficulty associated with following a GFD.

The finding that depression had the strongest, and in fact only independent, relationship with reduced QOL is consistent with previous research across a wide range of populations (38). The results demonstrate that psychological factors are an important consideration, over and above the impact of gastrointestinal symptoms when investigating QOL in individuals with CD. The significant relations observed between gastrointestinal symptoms and psychological symptoms also support the suggestion that the presence of psychological symptoms may serve to intensify the perception of gastrointestinal symptoms, which together negatively impact QOL.

Also consistent with study one and previous research (37), the increased use of maladaptive coping strategies was more strongly related to decreased QOL than the reduced use of adaptive or task-oriented strategies, although not significantly so over and above the influence

of depression. That is, individuals who relied on distracting themselves from the difficult situation, denying the problem, or engaging in frequent self-blame in order to cope with the challenges of the GFD tended to have poorer QOL and higher levels of psychological symptoms. This was despite the finding that all of the adaptive strategies were used more frequently than the maladaptive strategies, and suggesting that interventions to improve QOL (and adherence) should focus explicitly on decreasing reliance on maladaptive strategies rather than merely boosting adaptive strategies, which most individuals with CD already seem to utilise.

In contrast to study one, the relationships between QOL and increased symptom duration and time to improvement, the presence of additional intolerances, and the reason for diagnosis (symptom-detected versus screen-detected) were not confirmed. One possible explanation for this is that participants who consented to participate in the second study (which subsequently involved completing a six-week intervention) may have been more invested in their health at baseline than the sample who were recruited for the simpler questionnaire study, with the former group having worked to overcome the potential negative impact of such disease characteristics on QOL.

Interestingly, the amount of variance in QOL accounted for by the CDQ was less than that accounted for by the number of symptoms experienced prior to diagnosis in study one. Despite this, the size of the correlations between gastrointestinal symptoms and psychological symptoms were similar across the two studies. Given that the participants in study two had relatively few/low severity symptoms at the time of assessment it is likely that symptoms had a lesser impact on QOL than the more severe symptoms experienced prior to diagnosis. Therefore in addition to the idea that psychological symptoms serve to exacerbate the perception of gastrointestinal symptoms, it may also be the case that symptoms prior to diagnosis have a

lasting negative impact on QOL via social and psychological functioning, which reduces as the incidence of such symptoms decreases. In both studies, however, the severity of gastrointestinal symptoms accounted for only a small amount of the variance in QOL, suggesting that the reductions in QOL seen in this population are the result of other factors – most notably psychological symptoms.

GENERAL CONCLUSIONS AND LIMITATIONS

Several limitations should be considered when interpreting these results. Firstly, recruitment via the Coeliac Society and the low response rates may have led to a self-selection bias, whereby members, and specifically those who chose to respond, may be more invested in their health and diet than the general CD population. This has been noted in other adherence studies (e.g., 21, 63); nonetheless, since it was relationships between the variables that were of interest, there is no reason to believe that these relationships would differ in a more or less satisfied/ adherent sample.

Secondly, the use of self-report measures of psychological symptoms also represents a limitation, as high scores do not necessarily indicate a diagnosable condition. Regarding adherence, although the use of a concurrent dietitian rated assessment would strengthen the findings, the use of the well-validated CDAT means the current results can be viewed with more confidence than previous research which has relied on simple measures (e.g., Likert and visual analogue scales) that do not correspond with more objective measures (64). Finally, the cross-sectional design means that the direction of causation between gastrointestinal and psychological symptoms, coping, adherence, and QOL is unclear. A longitudinal study is needed to confirm the complex and likely bidirectional relationships between these variables.

Notwithstanding these limitations this research is the first to investigate the combined impact of disease, psychological, and adherence factors on QOL in CD. It demonstrates that the presence of psychological symptoms (in particular depression) and an increased reliance on maladaptive coping strategies represent greater threats to achieving adequate QOL for individuals with CD than gastrointestinal symptoms. These results mirror those found in other disease populations (38), and highlight the importance of targeting both adherence to the GFD and psychological symptoms and coping in people with CD to minimise symptoms and maximise QOL outcomes, as has recently been demonstrated by the effectiveness of such an intervention in a randomised controlled trial (60).

References

1. Green PHR, Jabri B. Coeliac disease. Lancet. 2003;362:383-91.
2. Green PHR, Jabri B. Celiac disease. Annual Review of Medicine. 2006;57:207-21.
3. Green PHR, Cellier C. Celiac disease. The New England Journal of Medicine. 2007;357:1731-43.
4. Reilly NR, Green PHR. Epidemiology and clinical presentations in celiac disease. Seminars in Immunopathology. 2012;34:473-8.
5. Green PHR, Fleischauer AT, Bhagat G, Goyal R, Jabri B, Neugut AL. Risk of malignancy in patients with celiac disease. American Journal of Medicine. 2003;115:191-5.
6. Greco L, Romino R, Coto I, Di Cosmo N, Percopo S, Maglio M, et al. The first large population based twin study of coeliac disease. Gut. 2002;50:624-8.
7. American Autoimmune Related Diseases Association. The cost burden of autoimmune disease: The latest front in the war on healthcare spending. Eastpointe, Michigan: American Autoimmune Related Diseases Association; 2011.
8. Tack GJ, Verbeek WHM, Schreurs MWJ, Mulder CJJ. The spectrum of celiac disease: Epidemiology, clinical aspects and treatment. National Review of Gastroenterology and Hepatology. 2010;7:204-13.
9. Mustalahti K, Catassi C, Reunanen A, Fabiani E, Heier M, McMillan S, et al. The prevalence of celiac disease in Europe: Results of a centralized, international mass screening project. Annals of Medicine. 2010;42:587-95.
10. Fowell AJ, Thomas PW, Surgenor SL, Snook JA. The epidemiology of coeliac disease in East Dorset 1993-2002: An assessment of the 'coeliac iceberg' and preliminary evidence of case clustering. QJM. 2006;99:453-60.
11. West J, Logan RFA, Hill PG, Lloyd A, Lewis S, Hubbard R, et al. Seroprevalence, correlates, and characteristics of undetected coeliac disease in England. Gut. 2003;52:960-5.
12. Swinson CM, Levi AJ. Is coeliac disease under-diagnosed? British Medical Journal. 1980;281:1258-60.
13. Lee A, Newman JM. Celiac diet: Its impact on quality of life. Journal of the American Dietetic Association. 2003;103:1533-5.
14. Hauser W, Gold J, Stein J, Caspary WF, Stallmach A. Health-related quality of life in adult coeliac disease in Germany: Results of a national survey. European Journal of Gastroenterology and Hepatology. 2006;18:747-54.
15. Hallert C, Grännö C, Grant C, Hultén S, Midhagen G, Ström M, et al. Quality of life of adult coeliac patients treated for 10 years. Scandinavian Journal of Gastroenterology. 1998;33:933-8.
16. Fera T, Cascio B, Angelini G, Martini S, Guidetti CS. Affective disorders and quality of life in adult coeliac disease patients on gluten-free diet. European Journal of Gastroenterology and Hepatology. 2003;15:1287-92.
17. Usai P, Manca R, Cuomo R, Lai MA, Boi MF. Effect of gluten-free diet and co-morbidity of irritable bowel syndrome-type symptoms on health-related quality of life in adult coeliac patients. Digestive and Liver Disease. 2007;39:824-8.

18. Usai P, Minerbal L, Marini B, Cossu R, Spada S, Carpiniello B, et al. Case control study on health-related quality of life in adult coeliac disease. Digestive and Liver Disease. 2002;34:547-52.
19. Roos S, Hallert C. Psychological well-being of adult coeliac patients treated for 10 years. Digestive and Liver Disease. 2006;38:177-80.
20. Zarkadas M, Cranney A, Case S, Molloy M, Switzer C, Graham ID, et al. The impact of a gluten-free diet on adults with coeliac disease: Results of a national survey. Journal of Human Nutrition and Dietetics. 2006;19:41-9.
21. Cranney A, Zarkadas M, Graham ID, Butzner JD, Rashid M, Warren R, et al. The Canadian celiac health survey. Digestive Diseases and Sciences. 2007;52:1087-95.
22. Hallert C, Sandlund O, Broqvist M. Perceptions of health-related quality of life of men and women living with coeliac disease. Scandinavian Journal of Caring Sciences. 2003;17:301-7.
23. Casellas F, Rodrigo L, Lopez Vivancos J, Riestra S, Pantiga C, Baudet JS, et al. Factors that impact health-related quality of life in adults with celiac disease: A multicenter study. World Journal of Gastroenterology. 2008;14:46-52.
24. Hauser W, Musial F, Caspary WF, Stein J, Stallmach A. Predictors of irritable bowel-type symptoms and healthcare-seeking behavior among adults with celiac disease. Psychosomatic Medicine. 2007;69:370-6.
25. Johnston SD, Rodgers C, Watson RGP. Quality of life in screen-detected and typical coeliac disease and the effect of excluding dietary gluten. European Journal of Gastroenterology & Hepatology. 2004;16:1281-6.
26. Mustalahti K, Lohiniemi S, Collin P, Vuolteenaho N, Laippala P, Maki M. Gluten-free diet and quality of life in patients with screen-detected celiac disease. Effective Clinical Practice. 2002;5:105-13.
27. Nachman F, Mauri E, Cabanne A, Bai JC. Quality of life in celiac disease patients: Prospective analysis on the importance of clinical severity at diagnosis and the impact of treatment. Digestive and Liver Disease. 2009;41:15-25.
28. Barratt SM, Leeds JS, Sanders DS. Quality of life in coeliac disease is determined by perceived degree of difficulty adhering to a gluten-free diet, not the level of dietary adherence ultimately achieved. Journal of Gastrointestinal and Liver Disease. 2011;20:241-5.
29. Sainsbury K, Mullan B. Measuring beliefs about gluten free diet adherence in adult coeliac disease using the theory of planned behaviour. Appetite. 2011;56:476-83.
30. Nachman F, Planzer del Campo M, Gonzalez A, Corzo L, Vazquez H, Sfoggia C, et al. Long-term deterioration of quality of life in adult patients with celiac disease is associated with treatment noncompliance. Digestive and Liver Disease. 2010;42:685-91.
31. Addolorato G, Capristo E, Ghittoni G, Valeri C, Mascianà R, Ancona C, et al. Anxiety but not depression decreases in coeliac patients after one-year gluten-free diet: A longitudinal study. Scandinavian Journal of Gastroenterology. 2001;36:502-6.
32. Addolorato G, Leggio L, D'Angelo C, Mirijello A, Ferrulli A, Cardone S, et al. Affective and psychiatric disorders in celiac disease. Digestive Diseases. 2008;26:140-8.
33. Edwards-George J, Leffler DA, Dennis M, Franko DL, Blom-Hoffman J, Kelly CP. Psychological correlates of gluten-free diet adherence in adults with celiac disease. Journal of Clinical Gastroenterology. 2009;43:301-6.
34. Karwautz A, Wagner G, Berger G, Sinnreich U, Grylli V, Huber W-D. Eating pathology in adolescents with celiac disease. Psychosomatics. 2008;49:399-406.

35. Leffler DA, Edwards-George J, Dennis M, Schuppan D, Cook F, Franko DL, et al. Factors that influence adherence to a gluten-free diet in adults with celiac disease. Digestive Diseases and Sciences. 2008;53:1573-81.
36. Ciacci C, D'Agate C, De Rosa A, Franzese C, Errichiello S, Gasperi V, et al. Self-rated quality of life in celiac disease. Digestive Diseases and Sciences. 2003;48:2216-20.
37. Smith M, Goodfellow L. The relationship between quality of life and coping strategies of adults with celiac disease adhering to a gluten-free diet. Gastroenterology Nursing. 2011;34:460-8.
38. Skevington SM, McCrate FM. Expecting a good quality of life in health: Assessing people with diverse diseases and conditions using the WHOQOL-BREF. Health Expectations. 2010.
39. Fisher EB, Thorpe CT, McEvoy DeVellis B, DeVellis RF. Healthy coping, negative emotions, and diabetes management: A systematic review and appraisal. The Diabetes Educator. 2007;33:1080-103.
40. Masthoff ED, Trompenaars FJ, Van Heck GL, Hodiamont PP, De Vries J. Quality of life and psychopathology: Investigations into their relationship. Australian and New Zealand Journal of Psychiatry. 2006;40:333-40.
41. Moskovitz DN, Maunder RG, Cohen Z, McLeod RS, MacRae H. Coping behaviour and social support contribute indepedently to quality of life after surgery for inflammatory bowel disease. Diseases of the Colon and Rectum. 2000;43:517-21.
42. Rose M, Fliege H, Hildebrandt M, Schirop T, Klapp BF. The network of psychological variables in patients with diabetes and their importance for quality of life and metabolic control. Diabetes Care. 2002;25:35-42.
43. Katon W, Ciechanowski P. Impact of major depression on chronic medical illness. Journal of Psychosomatic Research. 2002;53:859-63.
44. Walker EA, Gelfand MD, Gelfand AN, Creed F, Katon W. The relationship of current psychiatric disorder to functional disability and distress in patients with inflammatory bowel disease. General Hospital Psychiatry. 1996;18:220-9.
45. Addolorato G, Mirijello A, D'Angelo C, Leggio L, Ferrulli A, Abenavoli L, 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. International Journal of Clinical Practice. 2008;62:1063-9.
46. Sainsbury K, Mullan B, Sharpe L. Gluten free diet adherence in coeliac disease: The role of psychological symptoms in bridging the intention-behaviour gap Appetite. 2013;61:52-8.
47. Murphy B, Herrman H, Hawthorne G, Pinzone T, Evert H. Australian WHOQOL instruments: Users manual and interpretation guide. Melbourne, Australia: Australian WHOQOL Field Study Centre; 2000.
48. Lovibond PF, Lovibond SH. The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scale (DASS) with the Beck Depression and Anxiety Inventories. Behaviour Research and Therapy. 1995a;33:335-43.
49. Lovibond SH, Lovibond PF. Manual for the Depression Anxiety Stress Scales (DASS). 2nd ed. Sydney, Australia: Psychology Foundation of Australia; 1995b.
50. Garner DM. Eating Disorder Inventory - 3. Professional Manual. Lutz, Florida: Psychological Assessment Resources, Inc.; 2004.
51. Endler NS, Parker JDA. Coping Inventory for Stressful Situations (CISS): Manual. 2nd ed. Toronto: Multi-Health Systems; 1999.

52. Leffler DA, Dennis M, Edwards-George J, Jamma S, Magge S, Cook EF, et al. A simple validated gluten-free diet adherence survey for adults with celiac disease. Clinical Gastroenterology and Hepatology. 2009;7:530-6.
53. Riedinger MS, Dracup KA, Brecht ML, Padilla G, Sarna L, Ganz PA. Quality of life in patients with heart failure: Do gender differences exist? Heart and Lung: The Journal of Acute and Critical Care. 2001;30:105-16.
54. Gray LJ, Sprigg N, Bath PM, Boysen G, De Deyn PP, Leys D, et al. Sex differences in quality of life in stroke survivors: Data from the Tinzaparin in Acute Ischaemic Stroke Trial (TAIST). Stroke. 2007;38:2960-4.
55. Coeliac Society of NSW. Gender breakdown. 2010.
56. Abdulkarim AS, Burgart LJ, See J, Murray JA. Etiology of nonresponsive celiac disease: Results of a systematic approach. American Journal of Gastroenterology. 2002;97(8):2016-21.
57. Ciclitira PJ, Moodie SJ. Coeliac disease. Best Practice & Research Clinical Gastroenterology. 2003;17:181-95.
58. O'Shea U, Abuzakouk M, O'Morain C, O'Donoghue D, Sheahan K, Watson P, et al. Investigation of molecular markers in the diagnosis of refractory coeliac disease in a large patient cohort. Journal of Clinical Pathology. 2008;61:1200-2.
59. Paarlahti P, Kurppa K, Ukkola A, Collin P, Huhtala H, Markku M, et al. Predictors of persistent symptoms and reduced quality of life in treated coeliac disease patients: A large cross-sectional study. BMC Gastroenterology. 2013;13:75.
60. Sainsbury K, Mullan B, Sharpe L. A randomized controlled trial of an online intervention to improve gluten free diet adherence in celiac disease. American Journal of Gastroenterology. 2013.
61. Hauser W, Gold J, Stallmach A, Caspary WF, Stein J. Development and validation of the celiac disease questionnaire (CDQ), a disease-specific health-related quality of life measure for adult patients with celiac disease. Journal of Clinical Gastroenterology. 2007;41:157-66.
62. Carver C. You want to measure coping but your protocol's too long: Consider the Brief COPE. International Journal of Behavioral Medicine. 1997;4:92-100.
63. Cranney A, Zarkadas M, Graham ID, Switzer C. The Canadian celiac health survey- The Ottawa chapter pilot. BMC Gastroenterology. 2003;3:8-13.
64. Leffler DA, Edwards-George J, Dennis M, Cook EF, Schuppan D, Kelly CP. A prospective comparative study of five measures of gluten-free diet adherence in adults with coeliac disease. Alimentary Pharmacology and Therapeutics. 2007;26:1227-35.

Table 1. Disease, psychological, and adherence characteristics of the study 1 sample

	Mean (SD)	Range	Relation to QOL (*r*)
Age (years)	44.2 (12.7)	18 – 69	0.03
Age at diagnosis (years)	37.4 (12.8)	1 – 64	0.03
GFD duration (years)	6.8 (7.2)	0.25 – 48	-0.03
Symptom duration (years)	9.9 (12.5)	0 – 60	-0.15**
Number of symptoms	5.92 (2.46)	0 – 11	-0.22***
	Category	% of sample	Relation to QOL (*t* or ρ)
Gender	Female	82.8	0.84
	Male	17.2	
Prompted diagnosis	Symptoms	74.4	-2.01*
	Screening	25.6	
Symptom recurrence	No symptoms	5.1	0.01
	Mild	15.9	
	Moderate	28.2	
	Severe	30.3	
	No gluten	20.5	
Time to improvement	Less than 1 week	13.8	-0.14**
	Less than 1 month	33.3	
	Up to 6 months	37.2	
	More than 6 months	11.0	
	No improvement	4.6	
Family history of CD		27.2	0.56
Additional dietary intolerances		24.6	3.81***
Comorbid medical conditions		32.8	1.51
	Mean (SD)	Range	Relation to QOL (*r*)
QOL	4.26 (0.77)	1 – 5	-
Depression	6.20 (8.18)	0 – 42	-0.56***

Anxiety	4.98 (6.16)	0 – 36	-0.43***
Stress	10.96 (9.29)	0 – 40	-0.46***
Eating disorder risk	27.27 (19.19)	0 – 91	-0.34***
Task-oriented coping	25.95 (4.89)	9 – 35	0.14**
Emotion-oriented coping	19.17 (6.40)	7 – 35	-0.37***
GFD adherence	12.31 (3.17)	7 – 31	-0.41***
Perceived difficulty	6.41 (0.75)	2.25 – 7	0.17**

Note: QOL = quality of life; SD = standard deviation; GFD = gluten free diet; CD = coeliac disease; * $p < .05$; ** $p < .01$; *** $p < .001$

Table 2. Summary of hierarchical regression analyses predicting QOL in study 1

Variable	*B*	*β*	R^2	*F*
Step 1				
Gender	0.90	0.04		
Number of symptoms	-0.75	-0.24***		
Symptom duration	-0.00	-0.06		
Time to improvement	-0.18	-0.24***		
Additional intolerances	-0.24	-0.13*		
Prompted diagnosis	-0.8	0.05	.131	8.60***
Step 2				
Gender	0.12	0.06		
Number of symptoms	-0.06	-0.20***		
Symptom duration	-0.00	-0.06		
Time to improvement	-0.12	-0.15**		
Additional intolerances	-0.25	-0.14**		
Prompted diagnosis	0.14	0.80		
GFD adherence	-0.09	-0.37***		
Perceived difficulty	0.05	0.05	.275	16.05***
Step 3				
Gender	0.13	0.06		
Number of symptoms	-0.04	-0.12*		
Symptom duration	-0.00	-0.05		
Time to improvement	-0.13	-0.18***		

Additional intolerances	-0.19	-0.11*		
Prompted diagnosis	0.12	0.07		
GFD adherence	-0.05	-0.22***		
Perceived difficulty	-0.01	-0.01		
Depression	-0.04	-0.38***		
Anxiety	-0.01	-0.05		
Stress	0.00	0.00		
Eating disorder risk	-0.00	-0.06		
Task-oriented coping	0.00	-0.00		
Emotion-oriented coping	-0.00	-0.03	.445	19.06***

Note: QOL = quality of life; GFD = gluten free diet; * $p < .05$; ** $p < .01$; *** $p < .001$

Table 3. Disease, psychological, and adherence characteristics of the study 2 sample

	Mean (SD)	Range	Relation to QOL (r)
Age at diagnosis (years)	42.1 (14.5)	1 – 73	0.03
GFD duration (years)	4.6 (7.0)	0.25 – 50	0.10
Symptom duration (years)	9.1 (13.2)	0 – 60	-0.12
	Category	% of sample	Relation to QOL (t or ρ)
Gender	Female	87.3	-0.77
	Male	12.6	
Prompted diagnosis	Symptoms	79.9	-0.17
	Screening	21.1	
Time to improvement	Less than 1 week		0.03
	Less than 1 month		
	Up to 6 months		
	More than 6 months		
	No improvement		
Family history of CD		24.3	
Additional dietary intolerances		33.9	-0.30
Comorbid medical conditions		35.4	-1.95
	Mean (SD)	Range	Relation to QOL (r)
QOL	4.24 (0.81)	1 – 5	-

Depression ^	5.94 (7.39)	0 – 42	-0.57***
Anxiety ^	4.72 (5.97)	0 – 32	-0.30***
Stress ^	9.35 (8.32)	0 – 40	-0.41***
Eating disorder risk ^	29.70 (20.48)	0 – 86	-0.11
Active	5.52 (1.87)	2 – 8	-0.11
Emotional support	4.39 (1.84)	2 – 8	0.14*
Instrumental support	4.38 (1.81)	2 – 8	0.02
Positive reframing	4.68 (1.82)	2 – 8	-0.04
Planning	4.99 (1.81)	2 – 8	-0.06
Acceptance	6.72 (1.51)	2 – 8	0.11
Self-distraction ^	3.29 (1.52)	2 – 8	-0.40***
Denial	2.34 (0.87)	2 – 8	-0.18*
Substance use ^	2.51 (1.04)	2 – 6	0.00
Behavioural disengagement	2.26 (0.68)	2 – 7	-0.21**
Venting ^	3.26 (1.20)	2 – 8	-0.14
Self-blame ^	2.83 (1.29)	2 – 8	-0.26***
Humour	3.64 (1.66)	2 – 8	0.03
Religion	2.87 (1.60)	2 – 8	-0.00
GFD adherence	12.20 (3.44)	7 – 28	-0.32***
Perceived difficulty	6.37 (0.84)	1.50 – 7	0.19**
Gastrointestinal symptoms [#]	39.24 (7.03)	18 – 49	0.17*

Note: QOL = quality of life; SD = standard deviation; GFD = gluten free diet; * $p < .05$; ** $p < .01$; *** $p < .001$; the mean QOL score was comparable to the average Australian population

norms (M = 4.3; SD = 0.8); scores for depression, anxiety, stress, and eating disorder risk fell in the normal/average ranges; mean adherence score is in the excellent or very good range (59.3% excellent or very good; 32.8% moderate; 7.9% fair-to-poor); ^ Significant correlations with gastrointestinal symptoms (depression: r = -0.19, p < .01; anxiety: r = -0.21, p < .01; stress: r = -0.22, p < .01; eating disorder risk: r = -0.18, p < .01; self-distraction: r = -0.22, p < .01; substance use: r = -0.20, p < .01; self-blame: r = -0.18, p < .05); # Females (M = 38.8; SD = 7.1) reported more severe gastrointestinal symptoms than males (M = 42.1; SD = 5.7; t = 2.18, p < .05).

Table 4. Summary of hierarchical regression analyses predicting QOL in study 2

Variable	*B*	*β*	R^2	*F*
Step 1				
Gender	0.21	0.09		
Gastrointestinal symptoms	0.02	0.18*	0.036	3.48***
Step 2				
Gender	0.23	0.10		
Gastrointestinal symptoms	0.01	0.09		
GFD adherence	-0.07	-0.28**		
Perceived difficulty	0.03	0.03	0.113	5.87***
Step 3				
Gender	0.15	0.06		
Gastrointestinal symptoms	0.01	0.07		
GFD adherence	-0.02	-0.07		
Perceived difficulty	0.02	0.02		
Depression	-0.06	-0.56***		
Anxiety	0.01	0.04		
Stress	-0.01	-0.06		
Eating disorder risk	0.01	0.14	0.352	12.20***

Note: QOL = quality of life; GFD = gluten free diet; * $p < .05$; ** $p < .01$; *** $p < .001$