Depression, symptoms, quality of life and diet quality in patients prescribed the RPAH Elimination diet

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Declaration

The candidate, Josie Ho, hereby declares that none of the work presented in this essay has been submitted to any other University or Institution for higher degree and that to the best of her knowledge contains no material written or published by another person, except where due reference is made in the text.

Signature

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Abstract

Aim: This study aimed to describe the distribution of depressive symptoms in patients prior to commencing the Royal Prince Alfred Hospital (RPAH) Elimination diet (ED), and investigate their association with symptoms, quality of life (QOL) and diet quality before and on the ED.

Methods: Depressive symptoms were assessed using the Beck Depression Inventory-II (BDI-II). Diet quality was assessed using the Healthy Eating Index for Australian Adults (HEIFA) before and on the ED.

Results: The majority of patients (71%) identified at low risk of depression (mean BDI-II score =10.5±9.0). A higher percentage of patients reported gastrointestinal (84%) and central nervous system (77%) symptoms more frequently, compared to skin (50%), respiratory (53%) and genitourinary (20%) symptoms. Median BDI-II score was higher in those reporting more frequent gastrointestinal (p=0.030), central nervous system (p=0.002), and genitourinary symptoms (p=0.015). No difference in median HEIFA before or on the ED; or change in HEIFA score between low and high risk depression groups. There was an association between BDI-II score and impact on QOL (p=0.005). Stomach pain/cramps, headache/migraine and fatigue were found to be associated with impact on QOL.

Conclusion: Distribution of depressive symptoms in patients before starting the RPAH ED was similar to the general adult population. There was a relationship between increasing symptom frequency and trend of increase of BDI-II score, with the presence of symptoms likely to prompt the increase in BDI-II score. Symptom type may as also be a determinant of this relationship.

Key words: depression, depressive symptoms, food intolerance, Elimination diet
Introduction

Food intolerances are non-immunological adverse food reactions which can be triggered by naturally occurring food substances (wheat, milk, and soy), chemicals (salicylates, amines, glutamates) and/or food additives (e.g. colours, flavourings, preservatives). Reactions occur due to irritation of nerve endings in different parts of the body. Symptoms vary from person to person and can affect the skin (urticaria, angioedema), respiratory system (sinus, breathing difficulties), gastrointestinal tract (bloating, diarrhoea) and/or central nervous system (headaches, migraines) with different severity and frequency. Food intolerance reactions are dose dependent and cumulative. Symptoms present when the chemical threshold is exceeded, after the gradual accumulation of food substances, chemicals and/or additives in the body. The onset of reaction is determined by individual’s threshold level. (1-3)

The Royal Prince Alfred Hospital (RPAH) Elimination Diet and Challenge Protocol (ED&CP) is a validated and effective diagnostic tool for food intolerance and includes three diet restriction levels: strict, moderate and simple. (2)

Depression is a common characteristic in patients suffering gastrointestinal (GIT) symptoms. (4, 5) Compared to the general population, higher prevalence of depression has been observed in patients who react adversely to food with GIT symptoms including coeliac disease (CD), irritable bowel syndrome (IBS) and food hypersensitivity. (6-8) Consistent with the pattern observed in general population, females demonstrated higher levels of depression than males in patients affected by GIT symptoms. (9) One study found that depression was more common in patients suffering IBS and CD than those
with food hypersensitivity. (10) Yet, all patients with these GIT symptoms had higher rates of depression than the general population.

Several studies in a range of medical conditions (e.g. inflammatory bowel disease (IBD), diabetes, head injury) have supported that patients with depression or anxiety have more physical symptoms than those without these psychological disorders such as GIT symptoms, headaches, dizziness and back pain. Furthermore, there is a dose-response relationship such that increased depressive or anxiety symptoms are related to increasing number of physical symptoms. (11-13) These studies demonstrate that the presence of depression or other psychological conditions might exacerbate the perception of physical symptoms. (14) In one study, Walker and colleagues found that patients affected by both IBD and depression had more severe GIT symptoms than those with IBD only. (11) Consistent with previous studies in other illness populations (11-14), Sainsbury et al confirmed the relationship between increased depression and more severe GIT symptoms in patients with CD. (15) Nachman and colleagues also found symptomatic CD patients had higher mean scores on the Beck Depression inventory (BDI), which is a validated tool to measure the severity of depression, than asymptomatic CD patients and the healthy population. (6)

Depression has been observed to have a strong and independent relationship with reduced quality of life (QOL) in a large range of populations. (16) Studies have found patients with CD have reduced QOL compared to the general population. (17-22) Sainsbury et al also found a significant correlation between reduced QOL and heightened depression in CD patients. Moreover, several studies demonstrated the correlation between reduced QOL and increased GIT symptoms severity in CD. (6, 23-27) Sainsbury et al found comparable results and also suggested that psychological and
GIT symptoms may jointly impact QOL. Further, the magnitude of the link with depression was found to be more strongly related to decreased QOL than GIT symptom severity. (15)

One study reported higher prevalence of depression in patients with IBS and food allergy than the healthy population. (7) Another study showed a higher prevalence of depression in patients having GIT complaints self-attributed to food hypersensitivity than the general population. (28) Lind et al suggested that psychological factors were not essential predictors of symptom severity in patients with subjective food hypersensitivity. (29) However, the correlation between depression and symptoms and their joint impact on QOL are still unclear and debatable due to the limited research in this field.

Treatment for food intolerance involves following a restrictive diet as does treatment for CD and other adverse food reactions including food allergy and food related IBS. While the correlation between depression, symptoms and QOL has been well established in CD, it has not previously been examined in adverse food reactions including food intolerance, food allergy and food related IBS.

A pilot study conducted at RPAH Allergy Unit identified that patients before commencing the ED&CP had a comparable distribution of depressive symptoms, as determined by mean BDI-II scores, compared with the general population (Debenham AJ, 2014; unpublished data). However, it is noted that small sample size of the study may limit the representative of the result for the target population. Therefore, this study aims to describe the distribution of depressive symptoms in patients at presentation with
larger population size, to investigate the association of depression and self-reported symptoms with QOL.

Furthermore, the field of research focusing on the relationship between overall diet quality and depression is new and the evidence is limited. Both Cross-sectional and observational studies suggest that diets higher in vegetables, fruits, legumes, whole grains and fish are associated with reduced risk of depression in adults. (30, 31) Higher adherence to the Mediterranean diet was shown to be associated with a decreased risk for depression. (32) These studies indicate that a possible association between dietary quality and depression may present. Therefore, this study also aims to investigate whether there is an association between depressive symptoms at baseline, and diet quality before and on the ED.

Methods

This study is part of a five-year observational study on the nutritional adequacy and dietary compliance of patients prescribed the RPAH ED&CP. Data used in this study was collected by previous research dietitians.

Patients with an initial appointment at the RPAH Allergy Unit were contacted by research dietitians via telephone one week before their appointment to screen for eligible patients. The inclusion criteria for the study were: aged ≥ 18 years, had presence of symptoms suspected to be food related, had suspected food intolerance with symptoms such as urticaria/angioedema, IBS, migraine or symptoms suspected to be food related.

Exclusion criteria for the study included anyone who had consulted with a dietitian at the Allergy Unit before for food intolerance and/or had completed the Elimination Diet
under a dietitian’s care. Eligible patients who were interested to join the study were emailed or mailed an information pack and a four-day weighed food record (WFR) which was to be completed prior to their initial appointment.

A Patient Information Form (PIF) and a series of psychological questionnaires (appendix) were given to patients to complete at their first appointment, after signing a consent form. Any incomplete data was clarified by research dietitians via telephone. Three weeks after initial appointment, an email reminder was sent regarding the completion of an on-elimination diet four-day WFR which was collected at their follow-up appointment. All data collected was entered by student research dietitians into Microsoft Excel 2007. FoodWorks8 and SPSS(33) were used for further data analysis.

The PIF is a self-reported questionnaire gathering demographic, social, dietary and clinical information. Symptom information was gathered using a question asking patients to rate the frequency as ‘never’, ‘occasionally’, ‘monthly’, ‘weekly’ or ‘daily’ and severity as ‘mild’, ‘mild to moderate’, ‘moderate’, ‘moderate to severe’ or ‘severe’. QOL information was gathered with a question asking patients to rate the impact of symptoms on QOL as ‘not at all’, ‘just a little’, ‘pretty much’ or ‘very much’.

The Beck Depression Inventory-II (BDI-II) is a 21-item self-reported and validated tool to assess clinical status of depression. BDI-II has different cut offs—0-13: minimal depression; 14-19: mild depression; 20-28: moderate depression; 29-63: severe depression. A BDI-II score of 13 was used as a cut off below which patients have a low risk of depression.(34)
Patient’s age, gender, weight, height, BDI-II score, self reported QOL, frequency and severity of presenting symptoms were extracted from the RPAH Allergy Unit electronic database.

Body Mass Index (BMI) was calculated from weight and height information and classified into 3 groups (underweight: <18.5, normal: 18.5-25, overweight/obese: >25).

Basic descriptive statistics were calculated in SPSS. All data was tested for normality using the Shapiro-Wilks test. For body system analysis, patients’ symptoms were grouped into two groups as ‘never/occasionally’ and ‘monthly/weekly/daily’. Mann-Whitney U test was to compare difference between BDI-II score for two symptom frequency groups.

For individual symptom analysis, patients’ symptom frequency and severity were analysed as five separate groups by ANOVA and Kruskal-Wallis H test with Tukey post-hoc test and Dunn’s non parametric comparisons respectively.

For QOL analysis, patient QOL was grouped into 3 groups as ‘not at all/just a little’, ‘pretty much’ and ‘very much’.

Healthy Eating Index for Australian Adults (HEIFA) is a scoring system developed to measure the diet quality based on the Dietary Guidelines for Australian Adults (DGAA) and Australian Guide to Healthy Eating (AGHE). The scoring mechanism of HEIFA measure the degree of compliance with the serving recommendation for various food groups/components including core food groups, discretionary foods and negative nutrients (e.g. saturated fat, added sugar, sodium or alcohol). The total HEIFA score ranges from 0 to 100. Higher scores represent higher compliance to the serving
recommendation. HEIFA was applied to the data from WFR so as to examine the diet quality of samples in this study.(35)

Ethics approval of this study was received from the Sydney Local Health District Human Research Ethics Committee (RPAH Zone), protocol No X13-0208.

**Result:**

A total of 197 patients had completed baseline BDI-II and were included in this study, with the majority being females (n=159, 81%). At baseline, the mean age of the total sample was 43±14; the mean BMI was 25.4±5.9 kg/m²; the mean BDI-II score was 10.5±9.0. 159 participants completed questions regarding presenting symptoms.

There were higher numbers of participant who reported “monthly/weekly/daily” than those reported “never/occasionally” in GIT and Central Nervous System (CNS) symptoms, whereas the distribution was comparable in skin and respiratory symptoms. In contrast, there were lower numbers of participant reported “monthly/weekly/daily” than those reported “never/occasionally” in genitourinary symptoms (Table 1).

71.1% participants were categorized to minimal depression, 14.7% were classified to have mild depression, 9.6% had moderate depression and 4.6% had severe depression. 28.9% patients showed high likelihood of depression. There was no difference in median BDI-II scores between males (9.0) and females (8.0; p=0.715) nor between three BMI groups (χ² (2)=4.327, p=0.115), with a mean rank BDI-II score of 88.6 for underweight group, 92.4 for normal weight group, 109.4 for overweight/obese group. (Appendix 1)
Less than 1% of patients reported QOL ‘not at all’ impacted; 14.3% reported QOL was impacted ‘just a little’; 44.2% reported QOL was impacted ‘pretty much’ and 40.9% reported QOL was impacted ‘very much’.

There was significant difference between overall HEIFA before and on the ED. The mean scores of overall HEIFA before and on ED were 53.4±7.5 and 58.5±9.2 respectively. A statistically significant increase of 5.1 was shown (t=4.039, p<0.001). There were no statistically significant differences in median HEIFA before, HEIFA on ED and in the difference of HEIFA (before & on ED) between males and females (p=0.27, p=0.49, p=0.26) or between the different BMI groups (p=0.30, p=0.93, p=0.38). (Appendix 2, Figure 1)

A Mann Whitney U test identified that there were statistically significant differences in median BDI-II score between the two frequency groups (‘never/occasionally’ and ‘monthly/weekly/daily’) for GIT symptoms (U=1124, p=0.030) (Figure 1c), CNS symptoms (U=1362.5, p=0.002) (Figure 1d) and genitourinary symptoms (U=1167.5, p=0.015) (Figure 1e). There was a trend of increase of BDI-II score when symptom frequency increased. However, the BDI-II score of most patients was still below 13 which represented a low risk of depression. There was no difference in median BDI-II score between symptom frequency groups for skin (U=2488, p=0.11) (Figure 1a) and respiratory symptoms (U=2631, p=0.72) (Figure 1b). Statistical data between symptoms, BDI and QOL are displayed in Table 2.

For individual symptom analysis, statistically significant differences in BDI-II score between the different frequency groups (‘never’, ‘occasionally’, ‘monthly’, ‘weekly’ & ‘daily’) were observed for nausea (X²(2)=13.872, p=0.008), wind/gas(X²(2)=17.617,
p=0.001), bloating/discomfort($X^2(2)=13.730, p=0.008$), stomach pain/cramps($X^2(2)=21.136, p=0.000$), diarrhoea($X^2(2)=13.215, p=0.010$) and fatigue($X^2(2)=28.362, p<0.001$) (Table 2). Dunn’s non parametric comparisons post hoc analysis identified statistically significant differences within frequency groups.

For nausea, there was higher median BDI-II score for those reporting monthly (median=12, $p=0.016$) symptoms compared to those that reported never experiencing nausea (median=5). (Figure 2.a)

Higher median BDI-II scores for those reporting wind/gas occasionally (median=9, $p=0.003$), monthly (median=10, $p=0.005$), weekly (median=7, $p=0.016$) and daily (median=10, $p=0.003$) were observed compared to those who reported never experiencing wind/gas (median=2.5) (Figure 2.b). There was a trend of increase of BDI-II score when symptom frequency increase. The increase between ‘never’ and ‘occasionally’ was more dramatic compared to the other groups.

Whilst higher median BDI-II scores for those reporting bloating/discomfort daily (median=12, $p=0.002$) symptoms presented compared to those who reported never experiencing bloating/discomfort (median=2) (Figure 2.c). Thus, there was a significant increase of BDI-II score from ‘never’ to ‘daily’, whilst the increase was not significant between other groups.

Furthermore, there were higher median BDI-II scores for those reporting stomach pain/cramps monthly (median=9, $p=0.035$), weekly (median=10, $p=0.001$), daily (median=12, $p=0.001$) than those who reported never experiencing stomach pain/cramps (median=3) (Figure 2.d). Overall there was a trend towards increasing BDI-II score with increasing symptom frequency.
Compared to those who reported never experiencing diarrhoea (median=5), higher median BDI-II score for those reporting weekly (median=10, p=0.042) symptoms was observed (Figure 2.e). In general, the BDI-II score increased when the frequency of diarrhoea increased.

Moreover, there were higher median BDI-II scores for those reporting fatigue weekly (median=10, p=0.009) and daily (median=12.5, p<0.001) compared to those who reported never experiencing fatigue (median=2). Whilst there was statistically significantly higher median BDI-II score for those reporting daily (median=12.5, p=0.001) than those reporting occasionally symptoms (median=5) (Figure 2.f). The trend of BDI-II score was elevating when frequency of fatigue increased.

For individual symptom analysis, statistically significant differences in BDI-II score between different severity groups (‘mild’, ‘mild to moderate’, ‘moderate’, ‘moderate to severe’ & ‘severe’) were observed on eczema (F=4.459, p=0.004), runny nose (F=4.531, p=0.012), asthma ($\chi^2(2)=10.032$, p=0.040) and fatigue ($\chi^2(2)=10.546$, p=0.032). Significant differences were identified for eczema, runny nose and asthma (see appendix), however no further conclusion can be drawn due to small sample size.

Whereas a post hoc analysis using Dunn’s non parametric comparisons identified statistically significantly higher median BDI-II scores for those reporting ‘moderate to severe’ (median=11, p=0.041) fatigue compared to those that reported ‘mild’ severity (median=5) (Figure 2.g). Overall, there was a trend of increase of BDI-II score when the fatigue severity increased.
There were no statistically significant differences in median HEIFA before, HEIFA on ED and difference of HEIFA between low and high risk depression groups (p=0.33, p=0.58, p=0.43). (Appendix 2, Figure 2)

Chi Square crosstabulations showed a significant association between BDI-II score and self-reported QOL (p=0.005). All patients identified at high risk of depression reported ‘pretty much’ or ‘very much’ on the self-reported QOL question. (Appendix 3)

Frequency of stomach pain/cramps, headache/migraine and fatigue were significantly associated with QOL (p=0.048, p=0.04, p<0.001). A higher proportion of patients in ‘monthly/weekly/daily’ groups reported ‘pretty much’ and ‘very much’ for the impact of QOL than those in ‘never/occasionally’ groups (Table 3). Due to the limited sample size, no conclusions could be drawn between QOL and frequency of symptoms (eczema, hives, swelling, rashes, hayfever, sneezing, runny nose, blocked nose, post nasal mucus drip, throat irritation, asthma, mouth ulcers, difficulty swallowing, vomiting, reflux, heartburn, muscle/joint aches and bladder/vaginal irritation) and severity of symptoms.

**Discussion:**

Unlike published studies in CD, IBS and food hypersensitivity, the distribution of depressive symptoms in patients prior to starting ED (10.5±9.0), as determined by BDI-II score, was analogous to that of the general adult population (12.6±9.9). (34) Majority of patients identified at low risk of depression.

The gender distribution in this study, with the majority being females, was consistent to previous study done at RPAH Allergy Unit (Debenham AJ, 2014; unpublished data), as well as studies in CD, IBS and other adverse food reactions. (6-8, 10, 15) Moreover,
females were found to have more depressive symptoms than males in those suffering
GIT symptoms including CD and IBS. (9, 10) However, result of the current study found
no significant BDI-II score difference between males and females. These finding on
gender difference in depressive symptoms may explain why more depressive symptoms
were found in patients with CD, IBS and other adverse food reactions (6-8, 10, 15), but
not in the current study.

More patients presented with GIT (84%) and CNS (77%) symptoms than skin (50%),
respiratory (53%) and genitourinary symptoms (20%), as determined by the percentage
of patients who reported symptom frequency as ‘monthly/weekly/daily’. Therefore, GIT
and CNS symptoms were relatively common in patients at presentation.

In terms of body system, the significant differences in BDI-II score between two
symptom frequency groups for GIT, CNS and genitourinary symptoms showed that the
risk of depression raised significantly when the symptom frequency increased. But the
depression risk was still below the subclinical level.

In CD patients, Sainsbury et al found more severe GIT symptoms at diagnosis were
associated with heightened depressive symptoms. (15) Nachman et al reported that CD
patients with GIT symptoms had significantly higher BDI-II score than those without
symptoms. (6) In this study, this pattern was not only observed in GIT symptoms but
also found in CNS and genitourinary symptoms.

However, as the relationship between increasing symptom frequency and increase of
BDI-II score was not observed for skin and respiratory symptoms, this shows that the
type of symptoms may be as a determinant of this relationship.
Individual symptoms were further investigated and results corresponded to the findings for body system. Overall there was a trend towards increasing BDI-II score with increasing symptom frequency for most GIT symptoms including nausea, wind/gas, bloating/discomfort, stomach pain/cramps, diarrhoea, as well as in CNS symptoms such as fatigue.

The overall increasing trend showed as GIT symptom frequency increased, the BDI-II score increased but not significantly. Yet, as the significant difference of BDI-II score was mostly observed between ‘never’ and other levels of frequency (occasionally, monthly, weekly or daily), this manifests that the presence of symptoms is likely to prompt the significant increase in BDI-II score. Limited conclusion can be drawn due to small numbers within each symptom frequency category (Figure 1.a-e) and there was no trend seen in GIT symptom severity.

Unlike GIT symptoms, similar trends for frequency and severity were observed for fatigue. Therefore, additionally psychological support for patients presenting GIT and CNS symptoms may be required, however requires further evidence.

For the majority of patients at presentation identified as low risk of depression, a relatively good diet quality was observed (HEIFA before=53.4±7.5). Similar characteristics were observed in one study about depression and diet quality. Jacka et al found individuals with past but not current depression, regardless of whether they have been previously treated, had a relatively good diet quality. (36)

Meanwhile, the significant increased HEIFA scores after commencing ED demonstrated the improvement of diet quality by ED. Previous research done at RPAH Allergy Unit revealed the increased HEIFA scores on the ED were because of the significant
increases in serves of unsaturated fats, and reduction in serves of non-cored foods, sodium intake, and saturated fats (Bessell E, 2016; unpublished data). The diet quality on ED was improved to be more in line with DGAA and AGHE compared to baseline.

No significant differences in HEIFA before or on the ED; or change in HEIFA score between low and high risk depression groups indicates the risk of depression may not relate to the diet quality in our group of patients. However, it is noticed that the representativeness of the result may be limited due to the small sample size (n=60).

Future research should focus on examining depressive factors, overall diet quality, and diet quality for each food component in a larger population group.

Consistent with findings in the literature for general population and CD patients (15, 16), the association between depressive symptoms and self-reported QOL was found in this study. All patients identified at high risk of depression reported ‘pretty much’ or ‘very much’ on the self-reported QOL question, whereas 80% of low risk depression group reported these options. The higher BDI-II scores patients had, the more impact on QOL patients suffered.

For most symptoms, no conclusions can be drawn with self-reported QOL due to small number of patients within each symptom frequency category. Future studies may wish to investigate the impact of symptom frequency and severity on QOL with a larger population. Despite this, the increase of frequency of stomach pain, headache and fatigue were associated with reduced QOL. These results were similar to findings in IBS patients. Cain et al revealed that abdominal pain had the biggest impact on QOL for women with IBS, compared to other lower GIT symptoms.(37) Spiegel et al found fatigue was related to reduced QOL in IBS patients.(38)
Furthermore, one study assessing the effect of pain on QOL recognised that pain, both acute and chronic, had negative impact on QOL.\(^{(39)}\) Considering the characteristics of stomach pain/cramps and headache, it is likely that pain has strong negative impact on QOL. Future studies may wish to examine the relationship between pain, fatigue and QOL in patients prescribed the RPAH ED, compared with other adverse food reactions such as IBS.

There are several limitations that should be considered when interpreting these findings. Firstly, sampling method may bias the results. Patients who had high risk of depression may be less likely to return the questionnaires, WFR or consent to the study where self-monitoring is involved.\(^{(40)}\) Voluntary participation may favour patients interested in this study and those with sufficient literacy and numeracy ability to complete the questionnaires and four-day WFR. Secondly, symptoms and QOL were self-reported, answers which may be influenced by one’s comprehension and context of the questions. Potential confounders such as socio-economic status and occupation should be considered when interpreting the findings from this study. Moreover, limited conclusions can be drawn when assessing the association between symptoms and QOL, due to the small number of participants in several symptom categories. Future studies may require more participants to provide an adequate sample size for each symptom category analysis.
Conclusion

This study confirmed the finding of past study done at RPAH Allergy Unit (Debenham AJ, 2014; unpublished data) by using a larger population and explored the association between depression, symptoms, QOL and diet quality in RPAH Allergy Unit patients. This provides a foundation for further investigation into the depressive symptoms and the association depressive symptoms have on symptoms, diet quality and QOL in patients prescribed RPAH ED, which will allows dietitians and physicians to tailor their advice and individualise supportive strategies.
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References


9. Simonds VM, Whiffen VE. Are gender differences in depression explained by gender

State and trait anxiety and depression in patients affected by gastrointestinal diseases:
psychometric evaluation of 1641 patients referred to an internal medicine outpatient

11. Walker EA, Gelfand AN, Gelfand MD, Creed F, Katon WJ. The relationship of
current psychiatric disorder to functional disability and distress in patients with

12. Lustman PJ, Clouse RE, Carney RM. Depression and the reporting of diabetes


14. Katon W. The impact of major depression on chronic medical illness. General

15. Sainsbury K, Mullan B, Sharpe L. Reduced quality of life in coeliac disease is more
strongly associated with depression than gastrointestinal symptoms. Journal of

16. Skevington SM, McCrate FM. Expecting a good quality of life in health: assessing
people with diverse diseases and conditions using the WHOQOL-BREF. Health


Appendices

Appendix 1 Distribution of The Beck Depression Inventory-II (BDI-II scores)

Figure 1. Distribution of BDI-II score between females and males before starting RPAH Elimination Diet (ED)

No gender difference in BDI-II score was found
Figure 2. Distribution of BDI-II score between three BMI groups before starting RPAH Elimination Diet. Y axis lines show cut-off at 13 below which patients have a low tendency/likelihood of depression.

There was no significant difference in mean rank BDI-II scores between ‘underweight’, ‘normal’ and ‘overweight/obese’ groups. A trend of increase of BDI-II score was observed but not significant (p=0.115).
Appendix 2 Distribution of Healthy Eating Index For Australian Adults (HEIFA) scores

Figure 1. Distribution of HEIFA scores between males and females a) HEIFA scores before ED, b) HEIFA scores on ED, c) The difference of HEIFA (before & on ED)

a)

b)
There were no significant differences in median HEIFA before, HEIFA on ED, and in the difference of HEIFA (before & on ED) between males and females (p=0.27, p=0.49, p=0.26).
Figure 2. Distribution of BDI-II scores between low and high risk of depression groups
a) HEIFA before, b) HEIFA on ED, c) difference of HEIFA (before & on ED)
There were no statistically significant differences in median HEIFA before, HEIFA on ED and difference of HEIFA between low and high risk depression groups (p=0.33, p=0.58, p=0.43).
Appendix 3 Association between BDI-II score and self-reported quality of life (QOL)

**Figure 1.** Number of patients in low and high depression risk groups, and further categorised to three QOL groups
All patients identified at high risk of depression reported ‘pretty much’ or ‘very much’ on the self-reported QOL question. Chi-square crosstabulations showed a significant association between BDI-II score and self-reported QOL (p=0.005).

**Figure Legends**

**Figure 1.** BDI-II scores compared to frequency of symptoms. (a) BDI-II scores versus frequency of skin symptoms. (b) BDI-II scores versus frequency of respiratory symptoms. (c) BDI-II scores versus frequency of Gastrointestinal (GIT) symptoms. (d) BDI-II scores versus frequency of central nervous system (CNS) symptoms. (e) BDI-II scores versus frequency of genitourinary symptoms. Number of patients in each category (n) was indicated under x axis. Y axis lines show cut-off at 13 below which patients have a low tendency/likelihood of depression. Mann-Whitney U test was used to compare the data. * indicates p<0.05; ** indicates p<0.01; *** indicates p<0.001.

**Figure 2.** BDI-II scores compared to frequency and severity of symptoms. (a) BDI-II scores versus frequency of nausea (b) BDI-II scores versus frequency of wind/gas. (c) BDI-II scores versus frequency of bloating/discomfort. (d) BDI-II scores versus frequency of stomach pain/cramps. (e) BDI-II scores versus frequency of diarrhoea.
BDI-II scores versus frequency of fatigue. (g) BDI-II scores versus severity of fatigue. Number of patients in each category (n) was indicated under x axis. Y axis lines show cut-off at 13 below which patients have a low tendency/likelihood of depression. * indicates p<0.05; ** indicates p<0.01; *** indicates p<0.001.
**Table 1.** Distribution of patients who reported “never/occasionally” or “monthly/weekly/daily” in different body symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Patients reported ‘never/occasionally’ n (%)</th>
<th>Patients reported ‘monthly/weekly/daily’ n (%)</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>77 (50)</td>
<td>76 (50)</td>
<td>153</td>
</tr>
<tr>
<td>Respiratory</td>
<td>69 (47)</td>
<td>79 (53)</td>
<td>148</td>
</tr>
<tr>
<td>Gastrointestinal (GIT)</td>
<td>24 (16)</td>
<td>130 (84)</td>
<td>154</td>
</tr>
<tr>
<td>Central nervous system (CNS)</td>
<td>35 (23)</td>
<td>118 (77)</td>
<td>153</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>114 (80)</td>
<td>29 (20)</td>
<td>143</td>
</tr>
</tbody>
</table>
Table 2. Statistical analysis information between symptoms, BDI and QOL

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Symptom frequency</th>
<th>Symptom severity</th>
<th>BDI</th>
<th>QOL</th>
<th>BDI</th>
<th>QOL</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>p value</td>
<td>p value</td>
<td>p value</td>
<td>p value</td>
<td>p value</td>
<td>p value</td>
</tr>
<tr>
<td>Skin</td>
<td>0.11</td>
<td>0.086</td>
<td>/</td>
<td>/</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eczema</td>
<td>0.23</td>
<td>-</td>
<td>0.004**</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hives</td>
<td>0.99</td>
<td>-</td>
<td>0.54</td>
<td>-</td>
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<td></td>
</tr>
<tr>
<td>Swelling</td>
<td>0.16</td>
<td>-</td>
<td>0.98</td>
<td>-</td>
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<td></td>
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<tr>
<td>Rashes</td>
<td>0.67</td>
<td>-</td>
<td>0.91</td>
<td>-</td>
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<tr>
<td>Respiratory</td>
<td>0.72</td>
<td>0.47</td>
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<td>Hayfever</td>
<td>0.44</td>
<td>-</td>
<td>0.12</td>
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<tr>
<td>Sneezing</td>
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<td>-</td>
<td>0.40</td>
<td>-</td>
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<tr>
<td>Runny nose</td>
<td>0.071</td>
<td>-</td>
<td>0.012*</td>
<td>-</td>
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<td></td>
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<tr>
<td>Blocked nose</td>
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<td>-</td>
<td>0.41</td>
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<tr>
<td>Post nasal mucus drip</td>
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<td>-</td>
<td>0.66</td>
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<td>Throat irritation</td>
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<td>-</td>
<td>0.91</td>
<td>-</td>
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<td></td>
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<tr>
<td>Nose/sinus problem</td>
<td>0.21</td>
<td>0.65</td>
<td>0.75</td>
<td>-</td>
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<td></td>
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<tr>
<td>Asthma</td>
<td>0.44</td>
<td>-</td>
<td>0.040*</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GIT</td>
<td>0.030*</td>
<td>-</td>
<td>/</td>
<td>/</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mouth ulcers</td>
<td>0.83</td>
<td>-</td>
<td>0.83</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty swallowing</td>
<td>0.11</td>
<td>-</td>
<td>0.77</td>
<td>-</td>
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<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>0.008**</td>
<td>0.057</td>
<td>0.15</td>
<td>-</td>
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<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>0.034*</td>
<td>-</td>
<td>0.11</td>
<td>-</td>
<td></td>
<td></td>
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<tr>
<td>Reflux (acid)</td>
<td>0.30</td>
<td>-</td>
<td>0.13</td>
<td>-</td>
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<td></td>
</tr>
<tr>
<td>Heartburn</td>
<td>0.57</td>
<td>-</td>
<td>0.47</td>
<td>-</td>
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<td></td>
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<tr>
<td>Indigestion</td>
<td>0.073</td>
<td>0.87</td>
<td>0.40</td>
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<td></td>
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<tr>
<td>Wind/gas</td>
<td>0.001**</td>
<td>0.097</td>
<td>0.63</td>
<td>0.19</td>
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<td></td>
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<tr>
<td>Bloating/discomfort</td>
<td>0.008**</td>
<td>0.49</td>
<td>0.31</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach pain/cramps</td>
<td>0.000***</td>
<td>0.048*</td>
<td>0.62</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>0.010*</td>
<td>0.32</td>
<td>0.54</td>
<td>0.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------</td>
<td>--------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>0.18</td>
<td>0.077</td>
<td>0.80</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>0.002**</td>
<td>-</td>
<td>/</td>
<td>/</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS</td>
<td>0.18</td>
<td>0.040*</td>
<td>0.19</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache/migraine</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.032*</td>
<td>-</td>
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<td></td>
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<tr>
<td>Fatigue</td>
<td>0.091</td>
<td>-</td>
<td>0.29</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle/joint aches</td>
<td>0.015*</td>
<td>-</td>
<td>/</td>
<td>/</td>
<td></td>
<td></td>
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<tr>
<td>Genitourinary</td>
<td>0.38</td>
<td>-</td>
<td>0.18</td>
<td>-</td>
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<td></td>
</tr>
</tbody>
</table>

*=p<0.05

**=p<0.01

***=p<0.001

-=no conclusion can be drawn due to small sample size

/=irrelevant
Table 3. Distribution of ‘not at all/just a little’, ‘pretty much’ and ‘very much’ in different frequency groups

<table>
<thead>
<tr>
<th>Individual symptoms frequency associated with QOL</th>
<th>Frequency groups</th>
<th>Percentage(%) of patients reported ‘Not at all/just a little’</th>
<th>Percentage(%) of patients reported ‘pretty much’</th>
<th>Percentage(%) of patients reported ‘very much’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach pain/cramps</td>
<td>‘never/occasionally’</td>
<td>22.0</td>
<td>44.1</td>
<td>33.9</td>
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<tr>
<td></td>
<td>‘monthly/weekly/daily’</td>
<td>7.7</td>
<td>47.4</td>
<td>44.9</td>
</tr>
<tr>
<td>Headache/migraine</td>
<td>‘never/occasionally’</td>
<td>21.0</td>
<td>45.2</td>
<td>33.9</td>
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<tr>
<td></td>
<td>‘monthly/weekly/daily’</td>
<td>6.2</td>
<td>47.7</td>
<td>46.2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>‘never/occasionally’</td>
<td>30.4</td>
<td>34.8</td>
<td>34.8</td>
</tr>
<tr>
<td></td>
<td>‘monthly/weekly/daily’</td>
<td>6.1</td>
<td>50.5</td>
<td>43.4</td>
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</tbody>
</table>
Figure 1. Distribution of BDI-II score between two frequency groups for a) skin symptoms, b) respiratory symptoms, c) gastrointestinal symptoms, d) central nervous symptoms, e) genitourinary symptoms
Figure 2. Distribution of BDI-II score between five frequency groups for a) nausea b) wind/gas, c) bloating/discomfort, d) stomach pain/cramps, e) diarrhoea, f) fatigue, g) distribution of BDI-II score versus five severity groups for fatigue