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Associations between diet quality and depression, anxiety, and fatigue in multiple sclerosis.

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Abstract

Background: Many people with multiple sclerosis (MS) modify their dietary intake post diagnosis, but there is little evidence that dietary modifications influence MS outcomes.

Methods: People with a first clinical diagnosis of central nervous system demyelination were followed annually for 10 years. Depression, anxiety, and fatigue were assessed at the 5-and 10-year reviews using the Hospital Anxiety and Depression Scale and Fatigue Severity Scale, respectively. Dietary intake in the preceding 12 months was assessed at baseline, and 5-and 10-year reviews using a food frequency questionnaire. We used the Australian Recommended Food Score (ARFS) and the Diet Quality Tracker (DQT) to assess diet quality.

Results: A higher diet quality in the previous 12 months using the ARFS score, but not the DQT, was associated with lower levels of depression (e.g., highest vs lowest quartile: β=-1.35,95%CI=-2.44,-0.26,p=0.01), but neither score was associated with anxiety or fatigue. After assessing diet quality prospectively with outcomes five years later, we found that higher ARFS score, but not DQT score, was associated with lower levels of subsequent anxiety and depression (highest vs lowest quartile; Anxiety: β=-1.61,95%CI=-2.76,-0.46,p=0.01, Depression: β=-1.25,95%CI=-2.44,-0.07,p=0.04), but not fatigue. No associations were observed between diet quality and subsequent change in depression and anxiety over five years, although an association was observed between diet quality and change in fatigue (e.g., highest vs lowest DQT quartile: β=-1.06,95%CI=-1.92,-0.21,p=0.02). When examining the cumulative effect of diet quality across the study period with our 10-year outcomes, only the cumulative DQT score was associated with depression but not anxiety or fatigue.

Conclusion: We found significant inverse associations between diet quality and depression and anxiety, but the effect sizes were modest and there was a lack of consistency between the

two diet quality measures (ARFS and DQT). A diet measure that correlates with diet quality might underlie our observed associations.

Introduction

Multiple sclerosis (MS) is a chronic degenerative and inflammatory disease affecting the central nervous system that results in a significant personal morbidity and economic burden to Australia (~$1.75 billion/year).[1] Depression, anxiety, and fatigue are common symptoms of MS that are strongly associated with health-related quality of life.[2]

Many people with MS modify their diet during their disease or follow specific suggested MS diet programs. However, there is limited evidence from high-quality studies showing that diet influences disease activity, disability progression, or MS-specific symptoms, much less the exact nature of a diet that would be beneficial. A 2020 umbrella review, collating studies on diet and MS, concluded that the evidence is primarily focused on the isolation of individual dietary components, many of which demonstrate no effect on outcomes of MS progression.[3] A 2020 review of clinical trials in MS identified 30 studies, many including supplementation, focusing on polyunsaturated fatty acid (PUFAs) supplements (11 trials), antioxidant supplements (10 trials), dietary programs (3 trials), and other dietary supplements (e.g., acetyl L-carnitine, biotin, creatine, palmitoylethanolamide, probiotics, riboflavin; 6 trials).[4] The authors stated that, at present, there is insufficient evidence to suggest that dietary interventions change the course of MS, and trials with whole foods were too heterogeneous for comparison.[4]

Rather than focusing on food groups, individual foods, or nutrients the use of composite diet indices may be an alternative to examine diet and MS outcomes. Composite diet scores have been developed to assess diet quality,[5] inflammation,[6] adherence to national dietary guidelines,[7,8] or adherence to a particular dietary pattern (e.g., Mediterranean diet,[9] or DASH diet to reduce blood pressure[10]). The use of an overall diet quality score has been successfully applied in chronic diseases such as cardiovascular disease, cancer, and type-2 diabetes, where a higher diet quality score was associated with a lower risk of disease.[11] In MS, a higher overall diet quality score has been associated with lower depression symptom scores and risk of depression in three observational studies involving prevalent cases,[12-14] but reverse causality could not be excluded in all studies. No association was observed with anxiety or fatigue.[14] Another cross sectional study (n=2469), found that a lower diet quality (Diet Habits questionnaire) was associated with a higher frequency of fatigue.[15] Long-term diet quality has also been associated with gut microbiome diversity,[16] which in turn has been associated with mental health disorders.[17] A high diet quality is recognised to be rich with foods such as vegetables and fruits (folates), fish (omega 3 fatty acids), vitamin C, vitamin E, and other carotenoid compounds (antioxidants) and these have been shown to influence the pathophysiology of mental health.[18-23]

In the Australian setting, two indices have been developed to assess diet quality: the Australian Recommended Food Score (ARFS)[24] and the Diet Quality Tracker (DQT).[5] Their designs differ in the food group and score allocation. To date, these tools have not been used in MS. We used a prospective study, where adults with a first clinical diagnosis of CNS demyelination were followed for 10 years, to examine the association between overall diet quality (assessed by the ARFS and DQT), and depression, anxiety, and fatigue in those who were diagnosed with MS by the 10-year timepoint. We hypothesised that higher diet quality would be associated with lower levels of depression, anxiety, and fatigue.

Methods

AusLong study - a prospective cohort study with over 10 years of follow-up

Case participants (n=282, aged between 18-59 years) were recruited into the Ausimmune Study, a multicentre case-control study. Participants entered the study with a first clinical diagnosis of central nervous system demyelination.[25] Subsequently, cases from the Ausimmune Study were followed in the Ausimmune Longitudinal (AusLong) Study. At follow-up, three participants were excluded because their presenting event was due to another neurological condition. Of the remaining 279 participants, 236 participated at the 5-year review and 225 at the 10-year review. For those who had converted to MS by the 10th year review (n=190), we captured diet data for 184 (96.7%), data on anxiety and depression for 179 (94.2%), and fatigue for 180 (94.7%) for those who had converted to MS by the 10-year review (n=190). Ethical approval of the study was provided by the Human Research Ethics Committees of the participating centres, and all participants provided written informed consent.

Diet, Nutrients, and Diet Quality

A semi-quantitative food frequency questionnaire, the Dietary Questionnaire for Epidemiological Studies (DQES v2), developed by the Cancer Council Victoria (Australia), was used to assess habitual dietary intake in the previous 12 months. We administered this questionnarie at the baseline, and at the 5- and 10-year reviews. Estimated daily intakes of most nutrients and total energy intakes were calculated by the Cancer Council[26] using tailored Australian food composition data.[27] For seasonal foods, participants were asked to record frequency as if the foods were in season.

To assess diet quality, two indices – the Australian Recommended Food Score[28] and the Dietary Quality Tracker[5] – were derived from the dietary intake data. We excluded those with implausible energy intakes (>20,000 and <3,000 kJ/day, n=2 for the 5-year review and n=11 for the 10-year review).

Australian Recommended Food Score (ARFS)

Diet quality was assessed using the ARFS following a method developed by Kant et al.[29] The ARFS provides a total score based on the intakes of vegetables, fruit, protein foods, grains, dairy, fats, and alcohol.[24] Higher scores were achieved by reporting the recommended serves of the specified food groups as well as a variety of fruit and vegetables.[24] In brief, points are awarded for specific portion sizes and frequency of consumption of food and beverage items within the food groups (Supplementary Table 1).[24] The total ARFS score is calculated by summing the total number of points for each food group (maximum 74).

Diet Quality Tracker (DQT)

The DQT provides an overall diet quality score, which has been used in studies of another chronic disease, type-1 diabetes.[30] The food groups comprising the DQT represent those in the Australian Guide to Healthy Eating, demonstrating suitability for assessing Australian cohorts.[5] The food groups used in the DQT are based on the Australian Dietary Guidelines five food groups including starchy and non-starchy vegetables, grains, fruit, legumes, milk/yogurt, protein rich foods, spreads/oils, alcoholic beverages, and discretionary food/beverages. As the published DQT protocol was designed for a nut intervention, nuts were excluded from the scoring. However, with the guidance of one of the original DQT authors (YP), we modified the points system to include nuts, and incorporated recent updates to the single-serve equivalents noted in the Australian Guide to Healthy Eating. In brief, dietary intake data (g/day) were converted to energy (kJ/day) using the AUSNUT 2011-13 composition database.[27] The intakes of individual foods (in kJ/day) were assigned to food groups and summed to create food group sub scores (in kJ/day). Each food group sub score was divided by the respective single serve equivalent (kJ) and points were awarded by the number of single serve equivalents of each food group (Supplementary Table 2).[5] The total DQT score is the sum of the calculated points for each food group (maximum 56 points).

Outcome measures

The Hospital Anxiety and Depression Scale (HADS-D and HADS-A Scores; 7 item scale, rating 0-3) was used to assess the severity of depressive and anxiety symptoms at the 5- and 10-year reviews. [31] An overall score (0-21) was established by summing individual scale items and the HADS has been validated in people with MS.[32]

The Fatigue Severity Scale (FSS; 9 item Likert scale, rating 1-7 developed for use in MS populations)[33] was used to assess the severity of fatigue symptoms at the 5- and 10- year reviews. Scores were averaged to realise a total FSS score ranging 1-7. Before answering the FSS, participants answered whether they experienced any symptoms of fatigue (yes/no). If they did not experience symptoms of fatigue, they were given an FSS score of 0.

Other measures

The Ausimmune baseline interview collected data on age, sex, and study location. Prospective annual reviews focused on changes since the previous review of habitual lifestyle and other factors (use of antidepressant and anxiolytic/sedative medications, medications use to treat fatigue, whether employed (yes/no), whether any changes in diet or supplement use since last review (yes/no), total number of days in the past 12 months of doing any vigorous physical activity of >10 minutes (modified version of International Physical Activity Questionnaire[34]), median weekly income ($AUD), education status, smoking status and presence and severity of 16 stressful life events (modified version of the Social Readjustment Rating Scale[35], summed to total number, number of positive events, number of negative events).

Face-to-face interviews by a study nurse and neurologist were conducted at the baseline, 5- and 10- year reviews. A study nurse assessed height and weight, used to calculate body mass index (BMI, weight in kg/height in m^2); a study neurologist assessed current disability by the Expanded Disability Status Scale (EDSS) at the time of review[36] and the number of relapses since previous face-to-face review. The treating doctor's notes were obtained to identify and verify relapses.

Statistical analysis

To assess diet quality in the previous 12 months and depression, anxiety, and fatigue, we examined whether diet quality at 5 and 10-year reviews was associated with HADS-D, HADS-A, or FSS at the 5 and 10-year reviews. To assess the prospective effects of diet quality, we examined whether diet quality at baseline and 5-year review were associated with HADS-D, HADS-A, or FSS five years later (5 and 10-year review, respectively). For both analyses we used transformed linear mixed-effects models for repeated measures with Box-Cox transformations; the results were back-transformed and presented on their original scale at the mean of model covariates. We used linear regression to examine whether diet quality at the 5-year review was associated with a subsequent change in HADS-D, HADS-A, or FSS from 5-year to the 10-year review.

To estimate the relative contributions of the current and past diet quality indices on depression, anxiety, and fatigue at 10-year review, the outcome values were regressed individually on covariates for the diet quality indices at baseline, 5 years, and 10 years. With the coefficients of individual diet quality indices showing a similar effect size and, thus importance, we fitted a final model using a single cumulative diet quality index that combined the three diet quality indices by taking the sum.[37, 38]

We used Pearson correlations to assess the association between the ARFS and DQT scores.

A one sample t-test was used to examine whether the mean diet quality score (DQT and ARFS) reduced over time among those who experienced a worsening of at least two points on the HADS-D (n=27) or HADS-A (n=31) between the 5- and 10-year reviews.

The section on 'other measures' describe the variables that were considered as potential confounders and we assessed these using directed acyclic graphs[39] (DAGitty[40]) and traditional methods based on the definition of confounding.[41 42,]

We adjusted for age, sex, total energy intake, and dietary reporting as a dichotomous term (under-reporters/over-reporters versus reliable reporters). Dietary reporting was based on the ratio of total energy intake (EI) to basal metabolic rate (BMR) ratio (EI/BMR). BMR was calculated using the Harris and Benedict[43] equation. Under-reporters were defined by Goldberg cut-offs using an EI/BMR ratio less than 0.87; reliable reporters between 0.87-2.75, and over-reporters above 2.75.[44]

All analyses were completed using STATA/SE 16.1 (StataCorp LP, College Station, USA).

Results

Table 1 shows the characteristics of the cohort at the 5- and 10-year reviews. The ARFS ranged from 10 to 52 and the DQT ranged from 8 to 35 at the 5-year review (Table 1). There was moderate correlation of 0.36 (p=0.01) and 0.37 (p=0.01) between the ARFS and DQT scores for the 5- and 10-year reviews, respectively.

Depression

A higher ARFS in the previous 12 months was associated with a lower depression score (*p*<0.001 for continuous variable). Those scoring >39 (highest quartile) had a mean HADS-D score that was 1.35 units lower than those scoring between 0 and 26 (lowest quartile, p_{trend}=0.02). The DQT demonstrated a comparable inverse trend with depression, but did not reach statistical significance (Table 2).

When assessing prospective effects, we found that there was no association between the ARFS and depression five years later as a continuous variable (Table 3). However, as a categorical variable, those scoring >39 having a mean HADS-D score that was 1.25 lower compared to those scoring between 0 and 26 (*p*=0.04). Again, the DQT showed a comparable inverse trend with depression, but did not reach statistical significance (Table 3).

There were no associations between the ARFS and DQT scores at the 5-year review and subsequent change in HADS-D from the 5 to the 10-year review (Supplementary Table 3).
When we examined the pattern of association between diet quality indices and level of depression at the 10-year review, we found no association between the cumulative ARFS score and HADS-D at the 10-year review; however, we did see an association with DQT (Table 4).

Each unit increase of the cumulative DQT score was associated with a -0.09 lower HADS-D at the 10-year review (*p*=0.03, Table 4).

Anxiety

There were no associations between either ARFS or DQT and HADS-A score in the previous 12 months (Table 2).

When assessing prospective effects, we found that a higher ARFS was associated with lower levels of anxiety five years later (p_{trend}=0.02), such that those with ARFS>39 had a mean HADS-A score that was 1.61 lower than those with AFRS≤26. The DQT showed a comparable inverse trend with HADS-A score, but this was not statistically significant (Table 3).

There were no associations between the ARFS and DQT scores at the 5-year review and subsequent change in HADS-A score from the 5 to the 10-year review (Supplementary Table 3) and no associations between the cumulative diet scores with anxiety at the 10-year review (Table 4).

Fatigue

There were no associations between the ARFS or DQT with the FSS score in the previous 12 months (Table 2).

Similarly, when assessing prospective associations, there were no associations between the ARFS or DQT at baseline and 5-year review and FSS five years later (5 and 10-year reviews, respectively; Table 3).

There were no associations between the ARFS and subsequent change in fatigue (Supplementary Table 3). While we observed some significant associations between the DQT and subsequent change in FSS five years later, there was no dose-dependency.

There were no associations between the cumulative diet quality scores with fatigue at the 10-year review (Table 4).

Reverse causality and heterogeneity

For both those with a worsening in HADS-D and those with a worsening in HADS-A, the mean ARFS did not significantly change between the 5- and 10-year reviews (worsened HADS-D: mean ARFS 5-year review 31.5, 10-year review 31.9, p=0.62 for difference; HADS-A: mean ARFS 5-year review 30.9, 10-year review 31.9, p=0.77 for difference). To examine the potential heterogeneity in the magnitude of associations with the 5-year review and with the 10-year review, we examined these separately, but found no difference (data not shown).

Discussion

In this prospective study of Australian adults with MS, we found some evidence that a higher diet quality was associated with a lower level of depression and anxiety, but the effect sizes were modest and there was a lack of consistency between the two diet quality measures. There was no convincing evidence that diet quality was associated with levels of fatigue.

For depression in the previous 12 months, we found that a higher overall diet quality as measured by ARFS was associated with a dose-dependently lower level of depression. Two large cross-sectional studies also found that a higher diet quality score was associated with lower depression scores in people with MS.[13, 14] Our effect size (-1.35 units in HADS-D), comparing the highest quartile to the lowest, was less than the previously described clinically important difference of 1.7 units.[45]

When we assessed the longer-term effects in relation to depression, we found that a higher ARFS was associated with a lower level of depression five years later, but there was no clear dose-reponse, and the association when we used the DQT score was weaker. We also found no association between diet quality on either scale and 5-year change in HADS-D score. When we examined the cumulative effect, we only found an association between the cumulative DQT score and HAD-D score at the 10-year review, but not for the cumulative ARFS score. A prospective study of 1,309 people with MS across several countries found a dose-response association between diet quality (Diet Habits Questionnaire) at baseline and lower frequencies of depression 2.5 years later. This same study, however, post adjustment found no association between diet quality at baseline and the risk of developing depression (Patient Health Questionnarie-2) over the 2.5 years follow up.[12] It is challenging to compare our study to this one, given the different measures of diet quality and dietary assessment used. However, it could be that the timing of dietary effect is modulating this association.

In relation to anxiety, we found that a higher diet quality (using the ARFS but not DQT) was associated with lower levels of anxiety five years later, but not when we examined subsequent 5-year change in anxiety or within our accumulation models. There was evidence of a dose response, and the effect size was close to the 1.7-unit difference considered as clinically important[45] (highest vs. lowest quartile -1.61 (-2.76, -0.46)). In a recent meta-analysis assessing the effect of dietary interventions in the general population, no overall effects on anxiety were observed (*RCT*=11, *n*=2270, Hedges g=0.100, 95% CI=−0.04 to 0.24, p=0.148) and a recent cross-sectional study found that a healthier diet was not associated with anxiety in people with MS.[14, 46]

We found no consistent evidence of associations between diet quality and fatigue in any analyses. While we observed some significant effects between the DQT score at the 5-year review and subsequent change in fatigue from the 5- to 10-year reviews (p=0.02), this was not observed for the ARFS, and no clear dose response was present. No associations were observed for cumulative diet scores. A recent review of dietary intervention studies in people with MS and identified four studies with a combined size of 146 participants.[47] The four dietary interventions were vastly different in nature (modified paleo diet, low fat diet, starchy plant food diet), with two studies part of a multimodal intervention, including physical activity (physical activity has been shown to reduce fatigue[48]). The authors concluded that dietary intake holds the potential to lower MS-related fatigue, but strong conclusions were not possible based on the existing evidence.[47] Our prospective study strengthens the evidence-base that diet quality does not materially influence fatigue in MS.[14]

The relative lack of consistency between results for the DQT and ARFS was unexpected. There was a modest correlation between the DQT and ARFS of about 0.36, suggesting that, although capturing similar constructs, they vary substantially. The two scales do handle food groups very differently. For example, the DQT differs from the ARFS as it separates starchy vs non-starchy vegetables, contains separate categories for legumes and discretionary foods, and assigns fewer points for higher consumption of protein rich foods and milk/yogurt. The lack of consistency raises the question of whether diet quality is the causal factor or whether there is another aspect of diet, which may be correlated with diet quality, underlying our observed associations. While it is thought that foods that enhance inflammation are considered to be low in diet quality (foods high in refined starches/grains, added sugars, total fats)[49], other foods such as red meat could be considered pro inflammatory in nature and for our analysis we scored higher diet quality (ARFS) with high serves of protein. If inflammation is indeed the underlying mechanism of diet quality, then diet quality may not be the best way of assessing dietary inflammation.[50] Indeed, we have seen that a more pro-inflammatory dietary pattern was associated with an increased risk of MS.[51]

Strengths of our study include the longitudinal design and the capability of looking at different temporal relationships. We were also able to examine a broad spectrum of environmental factors as potential confounders. Although we cannot fully rule out the possibility of reverse causality, to assess the possibility that poorer mental health may have resulted in poorer dietary choices, we examined whether the subgroups of participants who had a substantial change in their anxiety and depression scores also changed their diet quality, but this was not the case. While we captured 101 individual foods, mixed dishes, and beverages, some foods were unmeasured, such as soft drinks.

In conclusion, we found some associations between a higher diet quality and lower levels of depression and anxiety, but the effect sizes were modest and there was a lack of consistency between the two diet quality measures used. A dietary measure that correlates with diet quality might underlie our observed associations.

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Table 1. Characteristics of the participants in the AusLong Study

	5-year review		10-year review	
	n	**Mean (SD; Range)**	**n**	**Mean (SD; Range)**
Age (Years)	190	44.5 (9.7 ; 23.4-63.5)	190	48.65 (9.67; 27.85-68.15)
HADS Depression score change 5-10 years	168	-0.05 (2.77; -7.00-7.00)		
HADS Anxiety score change 5-10 years	168	-0.14 (3.32; -14.00-9.00)		
FSS change 5-10 years	180	0.04 (1.86; -5.78-5.56)		
DQT* Total Score	184	18.3 (4.5; 8.0-35.0)	183	18.55 (4.04; 9-29)
ARFS* Total Score	184	32.3 (9.5; 10.0-52.0)	183	31.74 (9.25; 7-52)
Days per week of vigorous physical activity in last 12 months	190	1.8 (2.0; 0.00-7.0)	190	1.66 (1.98; 0-7)
Height (cm)	190	166 (8; 148-187)		
Weight (kg)	188	76.3 (18.0; 47.0-160.0)	187	77.74 (19.50; 46.2-170)
BMI (kg/m^2)	190	27.4 (5.9; 17.5-46.2)	190	27.90 (6.25; 17.52-49.73)
Total energy intake (kJ/day) – excluding those with implausible intakes	188	7087.9 (2562.50; 3091.9-17115.4)	179	6570.81 (2228.57; 3032.33-15699.60)
	n	**Median (IQR)**	**n**	**Median (IQR)**
HADS Depression score*	179	4 (6)	188	3 (6)
HADS Anxiety score*	179	7 (5)	188	6 (5.5)
FSS*	190	4.78 (2.69)	189	4.78 (2.78)
Income total ($AUD per week)	180	699.50(1400)	173	699.50 (1449.50)
	n/N (%)		**n/N (%)**	
Female sex	153/190 (81)			
Study site**				
New South Wales	32/190 (17)			
Victoria	52/190 (27)			
Queensland	56/190 (29)			
Tasmania	49/190 (26)			
Employment Status				
Unemployed	8/190 (4)		3/190 (2)	
Home duties	30/190 (16)		18/190 (10)	
Part-time	61/190 (32)		63/190 (33)	
Full-time	62/190 (33)		52/190 (27)	

Disability Pension	20/190 (11)	36/190 (19)
Retired	8/190 (4)	16/190 (8)
Smoke ever (yes/no)	114/188 (77)	114/190 (60)
Disease modifying therapies (yes/no)	148/190 (79)	149/190 (78)
Any dietary supplement (yes/no)	127/190 (67)	154/190 (81)
Diet change over past year (yes/no)	73/190 (38)	70/190 (37)
Prevalence of Depression (HADS-D>7)	31/179 (17)	35/179 (20)
Prevalence of Anxiety (HADS-A>7)	94/179 (53)	76/179 (42)
Prevalence of Fatigue (FSS>5)	86/190 (45)	82/190 (46)

*HADS: Hospitality Anxiety and Depression Scale; FSS: Fatigue Severity Scale; BMI: Body Mass Index; ARFS: Australian Recommended Food Score; DQT: Diet Quality Tracker. FFQ: Food frequency Questionnaire.

** Cohort entry

Table 2: Diet quality in the previous 12 months: the association between the diet quality indices at 5-and 10-year reviews and depression, anxiety, fatigue at the 5- and 10-year reviews.

			Depression		Anxiety				Fatigue	
	N[5]	**N[10]**	**β*(95%CI)**	***p***	**β*(95%CI)**	***p***	**N[5]**	**N[10]**	**β*(95%CI)**	***p***
ARFS - Total Score Continuous form	171	170	**-0.07 (-0.11, -0.02)**	**<0.001**	-0.02 (-0.06, 0.02)	0.38	176	170	-0.01 (-0.04, 0.02)	0.61
ARFS - Total Score Categorical form										
0 - 26	52	47	0.00 (Ref)		0.00 (Ref)		52	48	0.00 (Ref)	
27 - 33	40	40	-0.85 (-1.84, 0.15)	0.10	-0.66 (-1.60, 0.27)	0.17	43	39	-0.30 (-0.97, 0.38)	0.39
34 - 39	35	46	-0.89 (-1.98, 0.19)	0.11	-0.09 (-1.15, 0.96)	0.86	35	46	0.24 (-0.58, 1.05)	0.56
>39	44	37	**-1.35 (-2.44, -0.26)**	**0.01**	-0.34 (-1.41, 0.74)	0.54	46	37	-0.30 (-1.08, 0.47)	0.45
Test for trend:				**0.02**		0.75				0.65
DQT - Total Score Continuous form	171	170	-0.08 (-0.18, 0.02)	0.13	-0.07 (-0.17, 0.03)	0.16	176	170	0.00 (-0.08, 0.07)	0.92
DQT - Total Score Categorical form										
0 - 16	51	41	0.00 (Ref)		0.00 (Ref)		52	42	0.00 (Ref)	
17 - 18	39	51	0.41 (-0.56, 1.38)	0.41	0.47 (-0.45, 1.40)	0.32	40	51	0.21 (-0.45, 0.88)	0.53
19 - 22	47	46	-0.24 (-1.21, 0.73)	0.63	-0.18 (-1.12, 0.76)	0.70	49	46	0.08 (-0.60, 0.75)	0.83
>22	34	32	-0.70 (-1.86, 0.45)	0.23	-0.22 (-1.38, 0.95)	0.71	35	31	0.19 (-0.67, 1.05)	0.66
Test for trend:				0.20		0.53				0.74

*Models were adjusted for energy intake, dietary reporting, age, and sex.
Transformed (box-cox; back transformed) linear mixed-effects models for repeated measures were used; **N[5]** and **N[10]** are the number of people in each category at the 5th and 10th year review, respectively. The same set of number apply to both depression and anxiety.

Table 3: Diet quality and outcomes five years later: the association between the diet quality indices at baseline and the 5-year review and depression, anxiety, fatigue at the 5- and 10- year review.

			Depression		Anxiety		Fatigue	
	N⁵	**N¹⁰**	**β*(95%CI)**	***p***	**β*(95%CI)**	***p***	**β*(95%CI)**	***p***
ARFS - Total Score [Continuous form]	112	119	-0.04 (-0.08, 0.01)	0.10	**-0.05 (-0.10, -0.01)**	**0.02**	0.00 (-0.04, 0.03)	0.81
ARFS - Total Score [Categorical form]								
0 - 26	27	31	0.00 (Ref)		0.00 (Ref)		0.00 (Ref)	
27 - 33	33	33	**-1.56 (-2.64, -0.47)**	**0.01**	**-1.46 (-2.54, -0.38)**	**0.01**	-0.37 (-1.19, 0.45)	0.37
34 - 39	22	21	**-1.41 (-2.63, -0.20)**	**0.02**	**-1.40 (-2.60, -0.19)**	**0.02**	-0.56 (-1.46, 0.33)	0.22
>39	21	34	**-1.25 (-2.44, -0.07)**	**0.04**	**-1.61 (-2.76, -0.46)**	**0.01**	-0.25 (-1.15, 0.65)	0.59
Test for trend:				0.10		**0.02**		0.64
DQT - Total Score [Continuous form]	114	119	-0.07 (-0.17, 0.03)	0.16	-0.07 (-0.17, 0.03)	0.19	-0.02 (-0.09, 0.06)	0.65
DQT - Total Score [Categorical form]								
0 - 16	26	34	0.00 (Ref)		0.00 (Ref)		0.00 (Ref)	
17 - 18	29	27	-0.76 (-1.81, 0.28)	0.15	-0.82 (-1.89, 0.24)	0.13	-0.04 (-0.81, 0.74)	0.93
19 - 22	31	33	-0.69 (-1.77, 0.38)	0.21	-0.78 (-1.87, 0.31)	0.16	0.02 (-0.76, 0.80)	0.96
>22	28	25	-0.94 (-2.12, 0.24)	0.12	-0.96 (-2.17, 0.24)	0.12	-0.04 (-0.93, 0.84)	0.92
Test for trend:				0.23		0.27		0.94

*Models were adjusted for energy intake, dietary reporting, age, and sex.

Transformed (box-cox; back transformed) linear mixed-effects models for repeated measures were used; $\mathbf{N^5}$ and $\mathbf{N^{10}}$ are the number of people in each category at the 5th and 10th year review, respectively. The same set of number apply to both depression and anxiety.

Table 4: The effect of diet quality accumulation across study period: the association between the cumulative diet quality scores and depression, anxiety, fatigue at the 10-year review.**

		Depression at 10- year review		Anxiety at 10- year review		Fatigue at 10- year review	
	N	**β*(95%CI)**	***p***	**β*(95%CI)**	***p***	**β*(95%CI)**	***p***
ARFS - Cumulative Score (47-149)	161	-0.01 (-0.04 - 0.02)	0.43	-0.05 (-0.11 - 0.01)	0.12	-0.00 (-0.04 - 0.02)	0.71
DQT - Cumulative Score (36-91)	161	**-0.09 (-0.17 - 0.01)**	**0.03**	-0.03 (-0.16 - 0.10)	0.66	-0.05 (-0.11 - 0.01)	0.11

*ARFS and DQT models were adjusted for energy intake, dietary reporting, age, and sex.

** Sum of the diet indices at baseline, year 5 and year 10.

Supplementary Table 1: Method for development of the Australian Recommended Food Score

Scoring method for foods listed in the Dietary Questionnaire for Epidemiological Studies (DQES) Version 2.

Food Group	Items giving 1 point	Australian Recommended Food Score
Vegetables	≥4 vegetables per day; potatoes cooked without fat; tomato sauce/paste/dried; tomatoes fresh/canned; capsicum; lettuce/endive/salad greens; cucumber; celery; beetroot; carrots; cabbage/brussels sprouts; cauliflower; broccoli; silver beet or spinach; peas; green beans; bean sprouts or alfalfa sprouts; pumpkin; onion or leeks; garlic; mushrooms; zucchini	22
Fruit	≥2 pieces of fruit/day; ≥1/week of each fruit or vegetable juice; canned or frozen fruit; oranges or other citrus; apples; pears; bananas; melons (water, rock, honeydew); pineapple; strawberries; apricots; peach/nectarines; mango/pawpaw; avocado.	14
Protein foods	Nuts; peanut butter or peanut paste; 1-4/week of each of beef; veal; lamb; pork; chicken; fish, steamed baked or grilled; fish, canned (salmon, tuna, sardines); ≥1/week of each of baked beans; soy beans/ soy bean curd/tofu; soya milk; other beans (chick peas, lentils); use up to 2 eggs per week.	14
Grains	≥1/week of each following bread types white high fibre; wholemeal; rye; multigrain; ≥4 slices of bread per day; ≥1/week all bran; sultana bran/fibreplus/branflakes; weetbix/vitabrits/weeties; rice; pasta/noodles vegemite/marmite/promite; cornflakes/Nutra grain/special; porridge; muesli.	14
Dairy	Reduced Fat or skim; > 500mL/day; Cheese ≤1/week; ice cream; yogurt ≥ 1/week; use ricotta/cottage cheese; use low fat cheese.	7
Fats	Use nil/polyunsaturated/monounsaturated margarine	1
Alcohol	Drink beer/wine/spirits <1/month up to 4 days/week; 1 or 2 glasses maximum/day	2

Supplementary Table 2: Method developing the Diet Quality Tracker score.

Food Group	Food Frequency Questionnaire items in food group	Single serve equivalent (kJ)	Serve size equivalent	Score awarded
Non starchy vegetables	peas; green; beans; beetroot; carrots; cabbage; cauliflower; broccoli; spinach; cucumber; celery; bean; sprouts; onion; mushrooms; zucchini; garlic; lettuce; capsicum	80	<1	0
			≥1<2	1
			≥2<3	2
			≥3<4	3
			≥4<5	4
			≥5	5
Grains	white bread; high fibre bread; white bread; rye bread; cornflakes; pasta; muesli; rice; pizza; Weet bix; bran flakes; all bran; multi grain bread; wholemeal bread; crackers	335	<1	0
			≥1<2	1
			≥2<3	2
			≥3<4	3
			≥4<5	4
			≥5	5
Fruit	Apples; bananas; tinned fruit; mango; melon; peaches; tomato; fruit juice; apricots; oranges; pears; pineapple; avocado	285	0	0
			>0<0.5	1
			≥0.5<1	2
			≥1<1.5	3
			≥1.5<2	4
			≥2	5
Legumes	baked beans; other beans; tofu	335	0	0
			>0<0.25	1
			≥0.25<0.5	2
			≥0.5<0.75	3
			≥0.75<1	4
			≥1	5
Milk/yoghurt	full cream milk; skim milk; reduced fat milk; ricotta; yoghurt; hard cheese; firm cheese; soft cheese; cream cheese; low fat cheese; soya milk	500	0	0
			>0≤2 or >4	1
			>2≤2.5	2

			>2.5≤3	3
			>3≤3.5	4
			>3.5≤4	5
Protein-rich foods	Beef; veal; lamb; bacon; chicken; ham; sausages; fried fish eggs; tinned fish	335	0	0
			>0≤2 or >3	1
			>2≤2.25	2
			>2.25≤2.5	3
			>2.5≤2.75	4
			>2.75≤3	5
Starchy vegetables	Potatoes; pumpkin	335	0	0
			>0≤0.125 or >1	1
			>0.125≤0.25	2
			>0.25≤0.5	3
			>0.5≤0.75	4
			>0.75≤1	5
Nuts	Nuts	800	0	0
			>0<0.25	1
			≥0.25<0.5	2
			≥0.5<0.75	3
			≥0.75<1	4
			≥1	5
Spreads/oils	Butter; margarine; peanut butter	200	0	0
			>0≤2 or >4	1
			>2≤2.5	2
			>2.5≤3	3
			>3≤3.5	4
			>3.5≤4	5
Alcoholic beverages	light beer; heavy beer; red wine; white wine; fortified wines; spirits	*10 g/d*	>2	0
			≤2	1
Discretionary foods/beverages	tomato sauce; sugar; meat pies; sweet biscuits; chocolate; ice cream; jam; crisps; cakes; hamburger; chips; flavoured milk; drink	600	>1	0
			≤1	1

Supplementary Table 3: Diet quality and subsequent 5-year change in outcome: the association between the diet quality indices at the 5-year review and change in depression, anxiety, fatigue from the 5- and 10- year review.

		Depression		Anxiety			Fatigue	
	N	**β*(95%CI)**	***p***	**β*(95%CI)**	***p***	**N**	**β*(95%CI)**	***p***
ARFS - Total Score Continuous form	186	-0.01 (-0.06, 0.04)	0.71	-0.03 (-0.09, 0.03)	0.28	186	0.00 (-0.04, 0.03)	0.77
ARFS - Total Score Categorical form								
0 - 26	54	+0.47 (-0.34, 1.27) (Ref)**		+0.32 (-0.66, 1.30) (Ref)**		55	+0.21 (-3.30, 0.73) (Ref)**	
27 - 33	45	-1.02 (-2.22, 0.17)	0.09	-0.68 (-2.13, 0.77)	0.35	44	-0.12 (-0.88, 0.64)	0.75
34 - 39	50	-1.03 (-2.27, 0.22)	0.10	-0.76 (-2.27, 0.75)	0.32	50	-0.48 (-1.29, 0.33)	0.24
>39	37	-0.43 (-1.65, 0.79)	0.49	-0.98 (-2.46, 0.51)	0.19	37	-0.16 (-0.94, 0.61)	0.68
Test for trend:			0.48		0.20			0.51
DQT - Total Score Continuous form	186	-0.03 (-0.14, 0.08)	0.54	+0.02 (-0.11, 0.15)	0.76	186	**-0.08 (-0.15, -0.01)**	**0.02**
DQT - Total Score Categorical form								
0 - 16	63	0.08 (-0.70, 0.86) (Ref)**		-0.04 (-0.98, 0.90) (Ref)**		64	0.53 (0.03, 1.02) (Ref)**	
17 -18	62	-0.91 (-2.15, 0.33)	0.15	-0.98 (-2.48, 0.53)	0.20	62	**-0.90 (-1.68, -0.13)**	**0.02**
19 - 22	27	-0.39 (-1.59, 0.82)	0.53	-0.33 (-1.78, 1.14)	0.66	27	-0.66 (-1.41, 0.09)	0.09
>22	34	-0.57 (-1.93, 080)	0.41	-0.26 (-1.91, 1.39)	0.76	33	**-1.06 (-1.92, -0.21)**	**0.02**
Test for trend:			0.49		0.82			**0.02**

*Models were adjusted for energy intake, dietary reporting, age, and sex.
**Results for categorical variables are presented as the mean absolute change (95% CI) of reference level of the predictor, then mean change (95% CI) of other levels relative to reference.