A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED)

Natalie Parletta [1], Dorota Zarnowiecki [1], Jihyun Cho[1], Amy Wilson [2], Svetlana Bogomolova [2], Anthony Villani[3], Catherine Itsiopoulos [4], Theo Niyonsenga [1,5], Sarah Blunden [6], Barbara Meyer[7], Leonie Segal [1], Bernhard T. Baune [8], Kerin O'Dea[1]

[1]Centre for Population Health Research, University of South Australia, GPO Box 2471, Adelaide, South Australia 5001, Australia, [2]Ehrenberg-Bass Institute for Marketing Science, University of South Australia, GPO Box 2471, Adelaide, South Australia 5001, Australia, [3]Faculty of Science, Health, Education and Engineering, University of the Sunshine Coast, 90 Sippy Downs, Sippy Downs, Queensland 4556, Australia, [4]Discipline of Dietetics and Human Nutrition, La Trobe University, Melbourne, Victoria 3086, Australia, [5]Centre for Research and Action in Public Health, Faculty of Health, University of Canberra, Canberra, Australian Capital Territory, Australia, [6]School of Human Health and Social Sciences, Central Queensland University, 44 Greenhill Road, Wayville, South Australia 5034, Australia, [7]School of Medicine, University of Wollongong, Northfields Avenue, Wollongong, NSW 2522, Australia, [8]Discipline of Psychiatry, School of Medicine, Royal Adelaide Hospital, University of Adelaide, Level 4, Eleanor Harrald Building, Adelaide 5005, Australia

Objectives: We investigated whether a Mediterranean-style diet (MedDiet) supplemented with fish oil can improve mental health in adults suffering depression.

Methods: Adults with self-reported depression were randomized to receive fortnightly food hampers and MedDiet cooking workshops for 3 months and fish oil supplements for 6 months, or attend social groups fortnightly for 3 months. Assessments at baseline, 3 and 6 months included mental health, quality of life (QoL) and dietary questionnaires, and blood samples for erythrocyte fatty acid analysis.

Results: $n = 152$ eligible adults aged 18–65 were recruited ($n = 95$ completed 3-month and $n = 85$ completed 6-month assessments). At 3 months, the MedDiet group had a higher MedDiet score ($t = 3.95$, $P < 0.01$), consumed more vegetables ($t = 3.95$, $P < 0.01$), fruit ($t = 2.10$, $P = 0.04$), nuts ($t = 2.29$, $P = 0.02$), legumes ($t = 2.41$, $P = 0.02$) wholegrains ($t = 2.63$, $P = 0.01$), and vegetable diversity ($t = 3.27$, $P < 0.01$); less unhealthy snacks ($t = -2.10$, $P = 0.04$) and red meat/chicken ($t = -2.13$, $P = 0.04$). The MedDiet group had greater reduction in depression ($t = -2.24$, $P = 0.03$) and improved mental health QoL scores ($t = 2.10$, $P = 0.04$) at 3 months. Improved diet and mental health were sustained at 6 months. Reduced depression was correlated with an increased MedDiet score ($r = -0.298$, $P = 0.01$), nuts ($r = -0.264$, $P = 0.01$), and vegetable diversity ($r = -0.303$, $P = 0.01$). Other mental health improvements had similar correlations, most notably for increased vegetable diversity and legumes. There were some correlations between increased omega-3, decreased omega-6 and improved mental health.

Discussion: This is one of the first randomized controlled trials to show that healthy dietary changes are achievable and, supplemented with fish oil, can improve mental health in people with depression.

Keywords: Mediterranean diet, Depression, Mental health, Quality of life, Fish oil, Omega-3, Omega-6, Intervention

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Introduction

The world is facing a growing epidemic of non-communicable diseases. In 2012, 68% of global deaths

(38 million) were attributable to non-communicable diseases, with cardiovascular diseases (CVDs) the leading cause.[1] The 2013 Global Burden of Disease report identified that, in both developing and developed countries, major depressive disorder now ranks as the second highest cause of years of life lost due to disability (YLD). From 1990 to 2013, YLD attributed to mental and substance abuse disorders increased by 45%, depressive disorders by 53.4% and CVDs by 89.2%,[2] constituting a major burden of disease worldwide with tremendous associated personal, psychosocial, and financial impacts.

It has long been known that people with CVD have a higher incidence of depression than the general population, and it is established that depression is a risk factor for developing CVD.[3] What is perhaps less recognized is that depression and CVD share similar underlying biological risk factors such as inflammation,[4–6] low levels of omega-3 polyunsaturated fatty acids (PUFAs)[7–9] and poor diets. Traditional Mediterranean diets, characterized by high intake of plant foods (vegetables, fruit, legumes, nuts, seeds, olives, wholegrains), extra virgin olive oil as the main culinary fat, moderate intake of fish and low intakes of confectionary, red meat, and processed food,[10] are emerging as protective for CVD.[11,12]

Meta-analyses of observational studies have shown that a healthy diet[13] and Mediterranean diet[14] are associated with lower risk of depression. People with mental illness have been identified as having poorer diet and other lifestyle behaviours that impact on health, and less understanding of the impact of lifestyle behaviours on health.[15] Randomized controlled trials (RCTs) such as the large Prevención con Dieta Mediterránea (PREDIMED) study have successfully implemented Mediterranean diets in adults with CVD risk.[16] Secondary analysis from the PREDIMED study showed some trends for reduced risk of depression in the MedDiet group[17] but was not powered for this outcome. We are aware of only two dietary RCTs in people with depression; this study[18] and another Australian study which was recently completed.[19]

Changing established dietary behaviours is challenging, and this is attributed to factors such an obesogenic environment[20] and the addictive nature of high-fat high-sugar foods.[21] However, there is evidence that neural reward thresholds can be changed in favour of preferring healthy over unhealthy food.[22] A Mediterranean diet not only has demonstrated health benefits but is also a highly palatable diet and thus more likely to become a sustainable part of a healthy lifestyle.[10]

We aimed to investigate the impacts of a Mediterranean-style diet intervention for mental health and quality of life (QoL) in people with depression using a RCT design over 3 months with follow-up at 6 months. Owing to the particularly low levels of omega-3 PUFAs in people with mental illness[23] including this sample,[24] we provided participants in the dietary intervention with fish oil supplements for 6 months. This paper reports the dietary changes that were achieved in a Mediterranean-style diet (MedDiet) intervention group versus a social (comparison) group, the impact on mental health, and correlations between improved mental health outcomes and changes in diet and erythrocyte (red blood cell) omega-3 and omega-6 PUFA concentrations.

Methods

The detailed study protocol is published elsewhere.[18] The trial was registered with the Australian New Zealand Clinical Trials Register (ACTRN12614000438651).

Participants

According to Cohen's power analyses,[25] at least 60 people in each group are required to detect a medium effect size with 80% power ($n = 120$) at the usual 5% significance level. Allowing for an estimated 30% dropout rate the target sample size was $n = 172$. We recruited 182 adults with either GP diagnosed or self-reported depression over the previous 2 months or more (which has a moderate level of agreement with diagnosed depression[26]) in 2014 and 2015 via the community using newspaper advertisements, flyers, television and radio interviews, social media, and a market research agency. Of those eligible volunteers, 163 attended baseline assessments. Eleven participants retrospectively identified after baseline assessments as not having a depression diagnosis or a 'moderate' to 'extremely severe' score on the depression subscale of the Depression Anxiety Stress Scale (DASS – see below) were excluded from analyses, leaving a total sample size of 152. A CONSORT flow chart of participants through the study is provided in Fig. 1.

Ethics, consent, and permissions

Ethics approval was provided by the Human Research Ethics Committee of the University of South Australia (Registration no. 0000032674) and all participants provided written informed consent to take part in the study.

Procedure

Interested volunteers were screened for eligibility by phone. Inclusion criteria were age between 18 and 65 years and diagnosed or self-reported depressive symptoms over the previous 2 months or longer. People who took fish oil supplements or had a high diet quality score on an adapted dietary screening tool were excluded. If participants were receiving treatment for
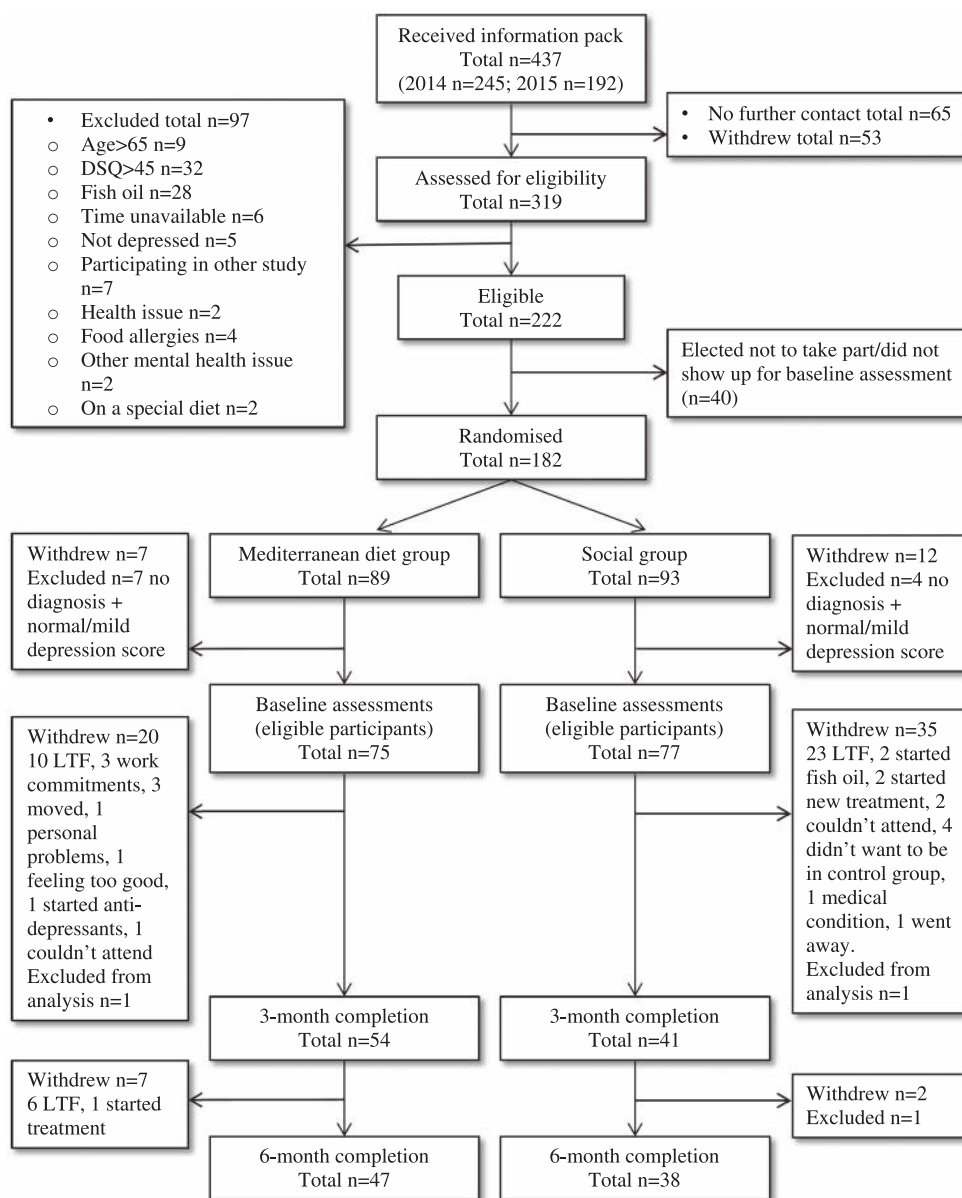
Figure 1   Consort flow chart of participants through the study. LTF = lost to follow-up; DSQ = dietary screening tool.

their depression they were asked to continue what they were doing. All participants were asked not to start any new treatment for the 6-month duration of the study. Eligible participants were sent detailed study information and a consent form via post or e-mail. On receipt of the signed consent form, they were scheduled to attend the Sansom Institute for Health Research clinic in Adelaide at the University of South Australia for baseline assessments. Before beginning baseline assessments participants were randomized by a team member not involved in screening or data collection to the MedDiet or Social group, blocked on age and gender, using the process of minimization.[27] Data collectors and participants were blinded to the treatment allocation until baseline assessments were completed. Investigators were blinded until after data were analyzed. Assessments were conducted at baseline, 3 and 6 months.

At baseline and 3-month assessments participants in the MedDiet group were given 3 months' supply of fish oil capsules (2 per day, grade EPAX 1050 TB each containing 450 mg DHA and 100 EPA). All participants were scheduled for fortnightly group sessions at the university campus for three months. For the MedDiet group's first visit they were given an interactive nutrition education session led by a dietitian, nutritionist and support study staff. For their subsequent fortnightly visits they took part in cooking workshops in a commercial kitchen at the university. Recipes focussed on simple, healthy, affordable, tasty meals using Mediterranean-style dietary principles. These had previously been trialled in cooking workshops in a pilot study with people suffering from severe mental illness, where positive dietary changes and improved cardiometabolic markers were achieved.[28] Following the cooking workshop,

MedDiet participants were given food hampers that provided ingredients for the recipe that had been cooked, and in addition including 500 ml extra virgin olive oil, vegetables, fruit, tinned legumes, tinned tomatoes, tinned tuna and mixed nuts (almonds, walnuts, hazelnuts). They were also given a link to a website that provided recipes, resources and cooking videos, and a printed book of recipes. The comparison group attended a fortnightly 'social' group with nibbles provided (i.e. biscuits, cheese, dips, tea/coffee, and water/juice), held in tutorial rooms at the university to control for the social interaction component of the cooking workshops. These groups undertook a range of social activities such as playing games, sharing holiday photos, book club activities, and completing personality questionnaires. Therapeutic discussion about depressive symptoms was discouraged, although many participants formed friendships as a result of the groups (similarly to the MedDiet group during cooking workshops).

Measures

The Depression Anxiety Stress Scale (DASS-21) and the Assessment of Quality of Life (AQoL)-8D scores were the primary outcome measures. Secondary outcome measures included the Positive and Negative Affect Scale (PANAS), 14-item Mediterranean diet questionnaire, and the Simple Dietary Questionnaire (SDQ). These are described below. A sociodemographic and health behaviour questionnaire collected information on age, gender, education level (1 = completed primary school to 8 = postgraduate degree), household income, and sleeping difficulties (how many hours of sleep on average on weeknights and weekends; and whether or not they consider sleep to be a problem – yes/no/don't know). Socioeconomic status was determined from participant postcodes using deciles of the Socio-Economic Indexes For Areas (SEIFA), a ranking of Australian neighbourhood disadvantaged and advantage, based on census data for variables such as education, income, and occupation status.[29]

DASS-21

The DASS is a 21-item self-report scale that provides a measure of the level of negative emotional states of depression, anxiety, and stress. It is a highly reliable measure with high convergent validity and good internal consistency with a Cronbach alpha of 0.82–0.93.[30,31] To identify degree of severity of these emotional states, DASS-21 sub-scale severity ratings were calculated based on the full DASS-42 severity rating[32] – each scale is multiplied by two and divided into severity categories to yield equivalent scores ranging from 1 (normal) to 5 (extremely severe) for clinical purposes.

AQoL-8d

The AQoL-8D is a 35-item questionnaire that is used to measure QoL. The 35 items load onto eight dimensions, of which three represent physical domains of QoL (independent living, pain, and senses) and five represent psychological domains (happiness, self-worth, coping, relationships, mental health). These load onto two super dimensions (physical and psycho-social). The scores from each dimension can be further combined to create a total AQoL-8D utilities score for use in economic evaluation. The AQoL-8D has good validity and internal consistency with alpha coefficients of 0.89–0.96.[33]

PANAS

The PANAS is a 20-item scale measuring positive and negative emotions. It has been validated and demonstrates reliable psychometric properties, discriminant, convergent and construct validity. The reliability (internal consistency) of the PANAS positive and negative emotions scales were previously determined to be $\alpha = 0.89$ and 0.85, respectively.[34]

Dietary questionnaires

A validated 14-item Mediterranean diet questionnaire was used to assess the level of adherence to the Mediterranean diet. Each item is scored as 0 or 1, yielding a maximum score of 14.[35] Higher scores on this questionnaire have been consistently associated with reduced risk of mortality from or incidence of CVD.[36]

A SDQ measured the frequency of intake of a range of food groups including, for the purpose of this study, vegetables, fruit, legumes, wholegrain foods, takeaway foods (examples given were unhealthy options such as burgers, chips, pizza), sweetened drinks, unhealthy sweet and savoury snacks, fish, meat/chicken and nuts. For each question a picture of the food was provided and the portion size was described. For each food group, frequency of usual intake was reported using six to nine-item response scales ranging from never/don't eat to consume seven or more serves per day. For vegetables, fruit, wholegrain foods, takeaway foods, snack foods, nuts, legumes, fish, and meat/chicken a further qualifying question presented a range of different items asking which of those had been consumed in the past 2 weeks, in order to help prompt memory about foods relevant to the previous item as well as to measure dietary diversity. For the purpose of this study diversity of fruit and vegetable consumption were measured because of the variety of bioprotective nutrients and phytonutrients provided by different fruits and vegetables.[37] Test–retest reliability of the SDQ over 1–2 weeks in a different sample ($n = 66$) ranged from $r = 0.690$ to $r = 0.875$ and validity coefficients with 24-hour recalls ranged

from $r = 0.256$ to $r = 0.569$ with the majority greater than $r = 0.400$ (unpublished). The SDQ will be further validated against 3-day food diaries which participants from the present study completed on two week days and one weekend day at baseline.

Omega-3 fatty acids

Fasted blood samples were used to measure erythrocyte levels of n-3 PUFAs to quantify and separate the direct contribution of fish oil supplementation to any improved outcome measures. Fasted blood samples were collected in 6 ml EDTA tubes, red blood cells were separated from plasma by low-speed centrifugation and packed red blood cells were stored in 1 ml micro tubes at $-80°C$ until analysis. Erythrocyte samples were thawed and prepared for fatty acid analysis according to Swierk *et al.*[38] using the direct transesterification procedure according to Lepage and Roy.[39] Samples were analysed by flame-ionization gas chromatography (model GC-17A, Shimadzu) using a $50 m \times 0.25 mm$ internal diameter capillary column. One microlitre of the sample was auto-injected into the column, and individual fatty acids were quantified using the Shimadzu analysis software (Class-VP 7.2.1 SP1, USA). Fatty acid peaks were identified by comparison with known fatty acid standards and quantitated by comparison to the 21:0 internal standard (Nu-chek and Sigma).

Statistical analysis

Analyses were performed using IBM SPSS Version 21.0 for Windows (Chicago, IL, USA). Descriptive statistics (mean and standard deviation, $M \pm SD$, or number/percentage for categorical variables, $n/\%$) were used to provide baseline participant demographics, and *t*-tests or Chi-Square (categorical outcome) to check for differences between randomized groups. Empirical distributions were examined for continuous outcome variables to ensure that assumptions of normality are met. To analyse primary and secondary outcomes and determine the effect of the Mediterranean diet intervention, a linear mixed modelling approach with variance component structure was used to compare changes in the MedDiet and social groups over time; this process includes all data therefore allowing analysis on an intent-to-treat basis. To investigate whether changed dietary patterns were associated with any positive outcomes in mental health, changes in diet scores, omega-3 and omega-6 PUFA levels were entered into Pearson correlation analyses with changes in mental health outcome scores.

Results

Participants included in the analyses (with depression diagnosis and/or DASS depression score in the 'moderate' to 'extremely severe' range) were comprised of 105 females and 47 males aged between 18 and 65 years ($M = 44 \pm 13$). This proportion reflects the approximate 2/1 ratio of depression incidence in women and men.[40] Thirty-eight per cent of participants reported a depression diagnosis and 36 per cent were taking anti-depressant medication. There was no statistically significant difference in age between those with ($M = 46.5 \pm 12.4$) and without ($M = 42.9 \pm 13.2$) a depression diagnosis ($P = 0.095$) and no significant difference in their baseline DASS depression score (22.60 ± 10.82 and 22.28 ± 8.53, respectively; $P = 0.841$) with both group means in the 'extremely severe' category (>14). Of those without a depression diagnosis, 86.4% ranked in the severe to extremely severe categories of the DASS depression scale compared with 86.0% of those with a diagnosis. Demographics and health-related data are broken down by treatment condition in Table 1. There were no statistically significant differences in demographic and health variables between groups, indicating successful randomization.

From the 152 eligible participants who commenced the study, 95 completed 3-month and 85 completed 6-month assessments (Fig. 1). Retention to 3 months

Table 1 Participant demographics and health status by treatment group ($n = 152$)

	Treatment $n = 75$	Control $n = 77$	P
Age ($M \pm SD$)	43.8 ± 12.8	44.6 ± 13.3	0.698
Gender	28% male	34% male	0.277
Race	93% Caucasian	90% Caucasian	0.412
Education			0.132
– completed years 8–12 (n)	12	20	
– completed post school qualifications (n)	63	57	
Household income per annum			0.862
– \$20 000–\$60 000 (n)	42	39	
– more than \$60 000 (n)	23	20	
SEIFA index ($M \pm SD$)	6.11	6.25	0.737
Marital status			0.670
– married or defacto (n)	33	34	
– separated/divorced/single (n)	18	22	
Depression diagnosis (n)[b]	24	33	0.167
Taking antidepressant medication (n)	24	30	0.338
DASS Depression score (M ± SD)	22.5 ± 10.6	21.3 ± 9.0	0.508
Sleep problems (n)	74	75	0.575

T-tests were used to compare continuous variables and Chi-square tests for categorical variables.
[a]SEIFA, a ranking of Australian neighbourhood disadvantage and advantage, based on census data for variables such as education, income and occupation status.
[b]Note that participants who did not have a diagnosis of depression were excluded if they reported symptoms in the normal-mild categories.

was 72% for the MedDiet group and 53% for the social group ($P = 0.013$). Retention to 6 months (from baseline) was 63% in the MedDiet group and 49% in the social group ($P = 0.068$). Most volunteers who did not complete the 3-month assessments dropped out before attending their first workshop/social group. There was no statistically significant difference in severity of baseline DASS depression scores between those who completed 3-month assessments ($M = 21.9 \pm 8.97$) and those who did not ($M = 23.3 \pm 10.15$; $P = 0.381$). There was also no statistically significant difference in age, gender, SEIFA index, education, or household income between those who completed or did not complete 3 months.

Dietary changes

Changes in diet from baseline to 3 and 6 months in each condition are provided in Table 2. Compared to the social group, the MedDiet group reported significantly greater increase in their total Mediterranean diet score[35] from baseline to 3 months (see Fig. 2), along with a significantly greater increase in consumption of vegetables, fruit, wholegrain foods, nuts and legumes, significantly lower consumption of unhealthy snacks and meat/chicken, and a greater diversity of vegetables. Both groups reported reduced sweetened drink intake which was not significantly different between the groups. These dietary changes were maintained at 6 months (Table 2).

Mental health outcomes

Both the MedDiet and the social group reported significantly improved mental health on all outcome measures (DASS, PANAS, and AQoL-8D subscales) over 3 months (all $P < 0.001$) except for the AQoL-8D pain value. Compared to the social group, the MedDiet group reported significantly greater improvement in their DASS depression score (Table 3, Fig. 3), and AQoL-8D mental health score over 3 months. Depression scores improved by 45% in the MedDiet group and 26.8% in the Social group – equating to 1.68 times greater improvement in depressive symptoms in the MedDiet group. All changes were sustained at 6 months (Table 3; Fig. 4).

Correlations between dietary changes and mental health changes over 3 months

Over 3 months there were several statistically significant correlations between improved diet and better mental health, as shown in Table 4. Higher Mediterranean diet scores were significantly associated with lower depression, anxiety, negative affect and better coping and overall QoL. Higher vegetable consumption was associated with less stress and more positive emotions and happiness while higher fruit consumption was associated with less anxiety and more positive emotions and relationships. Higher

intake of nuts was associated with reduced depression, anxiety and stress, and better mental health, self-worth and overall QoL. More legumes were associated with reduced anxiety, stress, negative emotions, and greater coping, psychosocial and overall QoL scores. Greater diversity of vegetables was associated with reduced depression, anxiety and negative emotions, and higher positive emotions, and along with greater diversity of fruits also with higher independent living, mental health, happiness, relationships, psychosocial and overall QoL. Reduced intake of takeaway food was associated with better pain and overall physical health QoL scores and reduced intake of unhealthy snacks was associated with improved mental health, coping and psychosocial QoL scores.

Correlations between erythrocyte polyunsaturated fatty acids and mental health

Correlations between changes in erythrocyte omega-3 and omega-6 PUFAs and mental health scores are shown in Table 5. Increased omega-3 PUFA eicosapentaenoic acid (EPA) was significantly associated with reduced anxiety and stress at 3 months and 6 months, and also with improved independent living, senses and physical health at 6 months. Increased omega-3 PUFA docosahexaenoic acid (DHA) was associated with reduced stress and negative emotions at 6 months. Decreased omega-6 PUFA arachidonic acid (AA) was associated with decreased stress and increased AQoL mental health, psychosocial and overall QoL at both 3 and 6 months as well as lower coping AQoL scores at 6 months. A reduced ratio of AA to EPA was associated with better pain, senses and physical health QoL scores at 6 months.

Discussion

Over three months the MedDiet intervention significantly and substantially improved the diet quality of people with self-reported depression when compared with diet changes in the social group, with higher total Mediterranean diet scores and increased intake of vegetables, fruit, wholegrains, nuts, legumes and greater diversity of vegetables, along with lower intake of unhealthy snacks and meat/chicken. These dietary improvements were sustained at 6 months. Both groups reported significantly improved mental health outcomes across all measures over 3 months which were also sustained at 6 months. The MedDiet group reported significantly greater improvements in depression and overall mental health-related QoL compared to the social group. Improvements in a range of mental health outcomes were significantly correlated with improvements in diet over 3 months, most notably for greater diversity of vegetables and fruit and intake of legumes but also including higher Mediterranean diet score, vegetables, fruit and nuts

Table 2 Mediterranean diet and food group scores in Mediterranean diet (MedDiet) and Social groups at baseline, 3 and 6 months, and test of differences between groups using linear mixed modelling, *n* = 152 (MedDiet *n* = 75; social group *n* = 77)

	Baseline M ± SD	3 months M ± SD	6 months M ± SD	Baseline to 3 months					3 months to 6 months				
				Estimate	SE	*t*-score	P	95% CI	Estimate	SE	*t*-score	P	95% CI
Mediterranean diet score[a]													
MedDiet	4.57 ± 0.24	7.08 ± 0.28	7.44 ± 0.32										
Social group	4.55 ± 0.24	5.20 ± 0.32	5.72 ± 0.36	0.95	0.24	3.95	<0.001**	0.47, 1.42	−0.22	0.42	−0.53	0.597	−1.06, 0.61
Vegetables													
MedDiet	1.73 ± 0.13	2.93 ± 0.15	3.07 ± 0.20										
Social group	1.74 ± 0.13	1.99 ± 0.17	2.27 ± 0.22	0.95	0.24	3.95	<0.001**	0.47, 1.42	−0.20	0.26	−0.75	0.454	−0.71, 0.32
Fruit													
MedDiet	1.35 ± 0.12	1.85 ± 0.14	2.02 ± 0.17										
Social group	1.38 ± 0.12	1.45 ± 0.15	1.42 ± 0.19	0.43	0.20	2.10	0.038*	0.02, 0.83	0.12	0.21	0.55	0.581	−0.30, 0.53
Wholegrain													
MedDiet	3.81 ± 0.47	5.49 ± 0.53	4.49 ± .56										
Social group	4.33 ± 0.47	3.92 ± 0.59	4.29 ± .62	2.09	0.80	2.63	0.010*	0.51, 3.67	−1.40	.84	−1.68	0.098	−3.07, 0.26
Takeaway food													
MedDiet	1.01 ± 0.18	0.73 ± 0.21	0.47 ± .21										
Social group	0.84 ± 0.18	0.87 ± 0.23	0.78 ± .23	−0.32	0.29	−1.07	0.29	−0.90, 0.27	−0.19	0.37	−0.51	0.61	−0.92, 0.54
Unhealthy snacks													
MedDiet	4.98 ± 0.56	2.70 ± 0.63	3.10 ± 0.55										
Social group	3.62 ± 0.55	3.30 ± 0.70	3.00 ± 0.61	−1.95	0.93	−2.10	0.038*	−3.79, −0.11	0.78	0.64	1.22	0.226	−0.49, 2.04
Sweetened drinks													
MedDiet	2.06 ± 0.38	1.24 ± 0.43	1.38 ± 0.38										
Social group	2.63 ± 0.38	1.62 ± 0.47	1.98 ± 0.42	0.19	0.59	0.32	0.752	−0.99, 1.37	−0.10	0.49	−0.20	0.841	−1.08, 0.88
Nuts													
MedDiet	2.13 ± 0.36	4.05 ± 0.41	4.10 ± 0.50										
Social group	1.40 ± 0.35	1.82 ± 0.46	1.58 ± 0.56	1.49	0.65	2.29	0.024*	0.20, 2.78	0.29	0.66	0.44	0.659	−1.03, 1.62
Legumes													
MedDiet	0.93 ± 0.18	2.35 ± 0.21	1.99 ± 0.27										
Social group	0.72 ± 0.18	1.25 ± 0.24	0.98 ± 0.30	0.90	0.37	2.41	0.017*	0.16, 1.64	−0.12	0.38	−0.31	0.759	−0.86, 0.63
Fish													
Intervention	0.79 ± 0.16	1.50 ± 0.19	1.32 ± 0.23										
Control	1.07 ± 0.16	1.43 ± 0.21	1.46 ± 0.26	0.34	0.33	1.03	0.307	−0.32, 0.99	−0.23	0.26	−0.89	0.376	−0.75, 0.29
Meat/chicken													
MedDiet	4.84 ± 0.38	3.23 ± 0.43	3.57 ± 0.34										
Social group	4.79 ± 0.37	4.46 ± 0.47	4.19 ± 0.48	−1.28	0.60	−2.13	0.035*	−2.48, −0.89	0.44	0.65	0.69	0.495	−0.84, 1.73
Vegetable diversity													
MedDiet	12.19 ± 0.66	16.90 ± 0.74	15.64 ± 0.83										
Social group	11.17 ± 0.66	12.57 ± 0.83	13.26 ± 0.94	3.31	1.01	3.27	<0.001**	1.30, 5.32	−2.18	0.96	−2.26	0.026*	−4.10, −0.26
Fruit diversity													
MedDiet	5.35 ± 0.41	7.20 ± 0.46	8.38 ± 0.59										

Continued

Table 2 Continued

	Baseline M±SD	3 months M±SD	6 months M±SD	Baseline to 3 months					3 months to 6 months				
				Estimate	SE	t-score	P	95% CI	Estimate	SE	t-score	P	95% CI
Social group	4.71 ± 0.40	5.37 ± 0.51	6.41 ± 0.67	1.19	0.66	1.81	0.073	−0.11, 2.49	0.03	0.66	0.04	0.967	−1.28, 1.34

*P < 0.05.
**P < 0.01.
[a]Mediterranean diet score out of 14. Food groups are derived from the SDQ; for each food group, frequency of intake was reported using six to nine-item response scales ranging from never/don't eat to consume seven or more serves per day. Vegetable and fruit diversity were calculated as the total number of different types vegetables and fruits consumed during the previous 2 weeks. CI = confidence interval (95%).
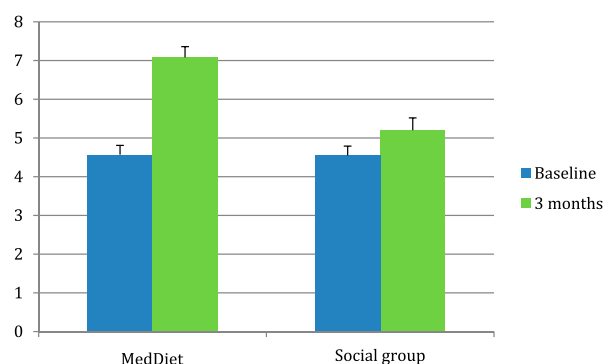

Figure 2 Mediterranean diet scores in each group at baseline and 3 months ($P < 0.001$). Bars represent standard error of the mean.

and reduced consumption of unhealthy snacks, take-away food, and meat.

The provision of free food has previously been shown to be successful in increasing intake. For instance, the PREDIMED study provided free nuts (walnuts, almonds, and hazelnuts) or olive oil to treatment groups, and showed that these groups consumed more of these foods.[16] This approach is compatible with behavioural economics and 'nudging' principles, i.e. using the path of least resistance, setting desirable defaults, making healthy food more available.[41] Along with education, goal setting, and menu ideas, continued exposure to and familiarity with healthy foods such as vegetables can increase liking and preference for that food.[42] Furthermore, learning basic cooking skills and hands-on learning of healthy recipes is empowering and has previously been associated with healthier food choices.[43,44] We successfully applied these strategies using the HELFIMED protocol in a pilot study for people with serious mental illness[28] and now in the present study. These skills, combined with the palatability and variety offered by a Mediterranean-style diet, may help to account for the sustained improvements shown over 6 months and potentially over the longer term.

To measure the impact of fish oil supplementation on mental health we measured erythrocyte omega-3 and omega-6 PUFAs. There were a small number of correlations between decreased AA (omega-6 PUFA), increased EPA and DHA and decreased ratio of AA/EPA and improved mental health over 3 and 6 months. We have observed previously that when fish oil is consumed and erythrocyte omega-3 PUFAs increase, the omega-6 levels decrease as they are displaced from the cell membranes.[45–47] Increased use of olive oil may have also reduced use of vegetable oils containing omega-6 PUFAs. The ratio of omega-6 to omega-3 PUFAs in cell membranes reflects dietary intake, which has a higher omega-6 to omega-3 ratio in Western diets compared to traditional diets globally[48] and in Australia.[49]

Table 3 Mental health and quality of life in Mediterranean diet (MedDiet) versus social groups at baseline, 3 and 6 months, and test of differences between groups using linear mixed modelling $n = 152$ (MedDiet $n = 75$; social group $n = 77$)

	Baseline $M \pm SD$	3 months $M \pm SD$	6 months $M \pm SD$	Baseline to 3 months					3 months to 6 months				
				Estimate	SE	t-score	P	95% CI	Estimate	SE	t-score	P	95% CI
Depression[a]													
MedDiet	23.00 ± 1.10	12.63 ± 1.26	12.50 ± 1.45										
Social group	21.79 ± 1.08	15.94 ± 1.45	15.28 ± 1.66	−4.52	2.02	−2.24	0.027*	−8.53, −0.52	−0.17	2.15	−0.08	0.936	−4.44, 4.09
Anxiety[a]													
MedDiet	14.08 ± 0.94	7.04 ± 1.05	6.17 ± 1.12										
Social group	14.49 ± 0.93	10.01 ± 1.18	8.68 ± 1.29	−2.56	1.43	−1.79	0.077	−5.40, 0.28	−0.64	1.35	−0.48	0.636	−3.33, 2.05
Stress[a]													
MedDiet	23.47 ± 0.97	13.96 ± 1.11	13.77 ± 1.31										
Social group	22.44 ± 0.96	15.98 ± 1.27	16.33 ± 1.50	−3.04	1.74	−1.75	0.082	−6.48, 0.39	−1.85	1.76	−1.05	0.297	−5.36, 1.66
Positive affect[b]													
MedDiet	23.31 ± 0.92	28.64 ± 1.06	28.31 ± 1.32										
Social group	22.55 ± 0.91	27.02 ± 1.23	27.63 ± 1.51	1.41	1.67	0.85	0.399	−1.89, 4.72	−0.76	1.73	−0.44	0.660	−4.19, 2.67
Negative affect[b]													
MedDiet	26.03 ± 0.85	19.67 ± 0.97	18.30 ± 1.08										
Social group	26.44 ± 0.84	21.62 ± 1.11	21.35 ± 1.23	−1.53	1.48	−1.04	0.302	−4.47, 1.40	−2.07	1.50	−1.39	0.170	−5.05, 0.90
AQoL Independent living[c]													
MedDiet	0.77 ± 0.02	0.87 ± 0.02	0.84 ± 0.02										
Social group	0.77 ± 0.18	0.83 ± 0.02	0.85 ± 0.03	0.04	0.02	1.46	0.148	−0.01, 0.08	−0.03	0.03	−1.21	0.231	−0.09, 0.02
AQoL Pain[c]													
MedDiet	0.68 ± 0.03	0.74 ± 0.03	0.74 ± 0.04										
Social group	0.71 ± 0.03	0.73 ± 0.39	0.72 ± 0.04	0.04	0.05	0.72	0.475	−0.06, 0.13	0.03	0.05	0.57	0.570	−0.07, 0.12
AQoL Senses[c]													
MedDiet	0.78 ± 0.02	0.88 ± 0.19	0.88 ± 0.02										
Social group	0.82 ± 0.02	0.85 ± 0.02	0.83 ± 0.02	0.06	0.03	1.93	0.056	−0.00, 0.11	0.02	0.03	0.77	0.444	−0.04, 0.09
AQoL Physical health[c]													
MedDiet	0.58 ± 0.03	0.70 ± 0.03	0.69 ± 0.03										
Social group	0.60 ± 0.03	0.67 ± 0.03	0.65 ± 0.04	0.06	0.04	1.53	0.129	−0.02, 0.13	0.02	0.04	0.43	0.668	−0.06, 0.09
AQoL Mental health[c]													
MedDiet	0.47 ± 0.01	0.61 ± 0.02	0.61 ± 0.02										
Social group	0.46 ± 0.01	0.55 ± 0.02	0.55 ± 0.03	0.06	0.03	2.10	0.037*	0.00, 0.11	0.01	0.03	0.09	0.930	−0.06, 0.06
AQoL Happiness[c]													
MedDiet	0.54 ± 0.02	0.67 ± 0.02	0.69 ± 0.03										
Social group	0.51 ± 0.02	0.63 ± 0.02	0.63 ± 0.03	0.01	0.03	0.18	0.856	−0.06, .07	0.02	0.03	0.76	0.449	−0.04, 0.09
AQoL Coping[c]													
MedDiet	0.53 ± 0.02	0.68 ± 0.02	0.69 ± 0.03										
Social group	0.53 ± 0.02	0.66 ± 0.02	0.64 ± 0.03	0.02	0.03	0.58	0.563	−0.05, 0.08	0.04	0.03	1.12	0.266	−0.03, 0.11
AQoL Relationships[c]													
MedDiet	0.55 ± 0.01	0.65 ± 0.02	0.67 ± 0.02										
Social group	0.54 ± 0.01	0.63 ± 0.02	0.63 ± 0.03	0.01	0.02	0.32	0.751	−0.04, 0.06	0.03	0.03	1.07	0.286	−0.02, 0.08
AQoL Self worth[c]													
MedDiet	0.58 ± 0.02	0.75 ± 0.02	0.75 ± 0.03										

Continued

Table 3 Continued

	Baseline M ± SD	3 months M ± SD	6 months M ± SD	Baseline to 3 months					3 months to 6 months				
				Estimate	SE	t-score	P	95% CI	Estimate	SE	t-score	P	95% CI
Social group	0.58 ± 0.02	0.69 ± 0.02	0.71 ± 0.03	0.05	0.03	1.68	0.095	−0.01, 0.12	0.01	0.03	0.33	0.745	−0.06, 0.08
AQoL Psychosocial super dimension[c]													
MedDiet	0.16 ± 0.02	0.31 ± 0.02	0.34 ± 0.03	0.03	0.03	1.03	0.307	−0.03, 0.10	0.03	0.03	1.04	0.301	−0.03, 0.10
Social group	0.14 ± 0.02	0.27 ± 0.02	0.26 ± 0.03	0.05	0.03	1.48	0.143	−0.02, 0.12	0.02	0.04	0.63	0.533	−0.05, 0.10
AQoL Utility Score[c]													
MedDiet	0.44 ± 0.02	0.63 ± 0.02	0.65 ± 0.03										
Social group	0.43 ± 0.02	0.58 ± 0.03	0.58 ± 0.04										

*P < 0.05.
**P < 0.01.
[a]DASS.
[b]PANAS.
[c]Assessment of Quality of Life (AQoL)-8d.
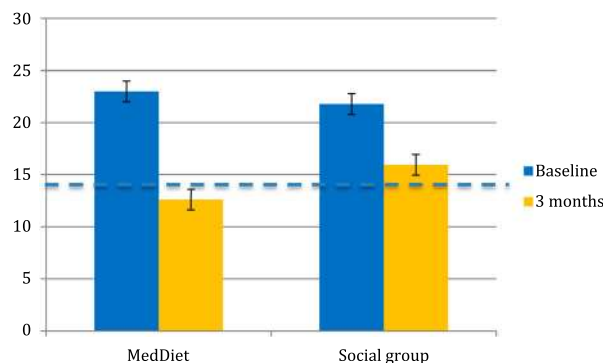
Figure 3 DASS depression scores in each group at baseline and 3 months (P = 0.027). Bars represent standard error of the mean. Dotted line represents cut-off for 'extremely severe depression'.

This can contribute to a pro-inflammatory state, given the inflammatory properties of eicosanoids produced by AA and anti-inflammatory properties of eicosanoids produced by EPA.[48] Furthermore, given the high concentration of DHA in neural membranes and its established role in a range of critical brain functions,[8] low omega-3 PUFA intake has been reflected in mental health outcomes[50] including depression.[51] The present study showed no significant correlation between increased omega-3 and improved depressive symptoms, although improved depression scores were associated with a decreased ratio of AA (omega-6) to EPA (omega-3). Improved depression was also significantly correlated with increased Mediterranean diet scores. A range of essential nutrients are required for healthy brain function and they also work synergistically; therefore improving the whole diet is likely to have far greater benefit for mental health than any single nutrient alone.[8] An interesting trial with elderly people with mild cognitive impairment recently discovered that reduced brain atrophy, and therefore risk of developing dementia, following Vitamin B supplementation was greatest in those adults who had adequate omega-3 levels.[52] This supports the contention that single nutrient trials are limited.
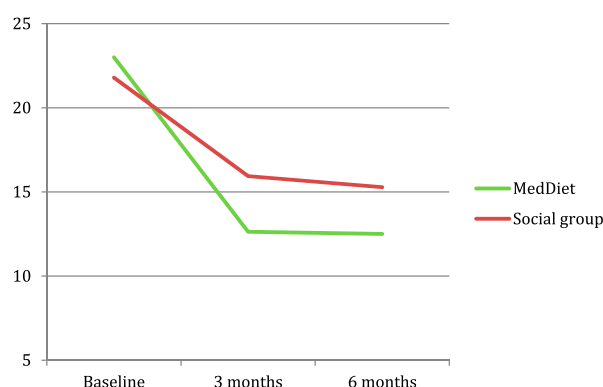

Figure 4 DASS depression scores at baseline, 3 and 6 months.

Table 4 Pearson correlations between changes in mental health and diet over 3 months ($n = 95$)

	Med	Veg	Fruit	Grains	T/away	Snacks	Drinks	Nuts	Legumes	Fish	Meat	Vegdiv	Fruitdiv
DASS depression	−.298**	−.137	−.191	−.049	−.040	.138	−.003	−.264*	−.196	−.124	.037	−.303**	−.148
DASS anxiety	−.238*	−.186	−.255*	−.198	−.013	.195	−.103	−.207*	−.253*	.024	.172	−.292**	.204
DASS stress	−.177	−.281**	−.151	−.011	−.017	.088	−.207*	−.280*	−.242*	−.033	.127	−.204	−.151
PANAS positive	.172	.224*	.228*	−.025	.035	−.039	−.064	.139	.203	.128	.115	.218*	−.159
PANAS negative	−.218*	−.155	−.151	−.092	.100	.121	−.025	−.155	−.273**	−.193	.081	−.231*	−.159
AQoL independent	.124	.025	.117	.110	−.046	−.165	−.190	.056	.060	.134	−.098	.327**	.271**
AQoL pain	.160	.092	.129	−.001	−.275**	.091	.037	.124	.105	.150	−.252*	.146	.056
AQoL physical health	.169	.092	.133	.031	−.248*	−.031	−.083	.096	.147	.151	−.177	.186	.185
AQoL mental health	.195	.176	.175	.049	−.073	−.232*	−.055	.221*	.257*	.170	−.091	.302**	.309**
AQoL happiness	.195	.253*	.152	.082	−.028	−.171	−.060	.155	.186	.074	.010	.295**	.304**
AQoL coping	.211*	.203	.174	.003	−.094	−.212*	−.148	.191	.277**	.108	.019	.195	.174
AQoL relationships	.109	.129	.216*	.011	−.053	−.184	−.160	−.001	.135	.071	.040	.270*	.208*
AQoL self-worth	.175	.139	.146	.083	−.160	−.156	−.099	.221*	.146	.030	−.092	.196	.170
AQoL psychosocial	.194	.179	.189	.042	−.079	−.297**	−.102	.150	.225*	.168	−.035	.297**	.303**
AQoL Utility score	.251*	.203	.165	.061	−.204	−.195	−.140	.183	.236*	.193	−.099	.323**	.276**

*$P < 0.05$.
**$P < 0.01$.
Note that all change scores are calculated as 3 months minus baseline. Med = Mediterranean diet score; Veg = vegetables; Grains = wholegrains; T/away = take away food; Snacks = unhealthy snacks; Drinks = sweetened drinks; Vegdiv = vegetable diversity; Fruitdiv = fruit diversity. AQoL = Assessment of quality of life. AQoL independent = independent living. A higher AQoL score = better quality of life on that scale.

Table 5 Pearson correlations between changes in mental health and erythrocyte PUFAs over 3 and 6 months

	3 months ($n = 95$)							6 months ($n = 85$)						
	AA	EPA	DHA	Total n-6	Total n-3	n-6/n-3	AA/EPA	AA	EPA	DHA	Total n-6	Total n-3	n-6/n-3	AA/EPA
DASS														
Depression	−.143	.213	.119	.027	.184	−.125	−.295**	.152	−.144	−.112	−.018	−.110	.065	−.041
Anxiety	.207	−.242*	.012	−.049	−.061	.045	.157	.201	−.241*	−.120	−.057	−.139	.081	.214
Stress	.267**	−.227*	−.158	−.123	−.207*	.097	.158	.259*	−.245*	−.226*	−.108	−.200	.098	.168
PANAS														
Positive	−.014	.049	−.066	.031	.065	−.066	.008	−.065	.051	.033	.099	.009	.056	.052
Negative	.114	−.087	−.057	−.174	−.034	−.051	−.030	.177	−.136	−.302**	−.037	−.210	.194	.043
AQoL-8D														
Independent[a]	−.132	.029	−.002	.084	.144	−.123	−.077	.062	.228*	−.001	−.040	.054	−.036	−.189
Pain	−.070	.040	−.005	.008	.075	−.068	−.077	−.070	.124	.137	−.033	.093	−.107	−.225*
Senses	−.167	.099	.015	−.049	.054	−.119	−.041	−.161	.274*	.163	.136	.059	.051	−.240*
Physical[b]	−.143	.213	.119	.027	.184	−.125	−.295**	−.098	.267*	.204	.001	.152	−.107	−.316**
Mental health	−.243*	.080	.138	.070	.143	−.039	−.054	−.245*	.122	.148	.043	.124	−.049	−.069
Happiness	−.139	.023	−.005	.079	−.027	.032	.060	−.203	.005	.065	.046	−.024	−.001	.002
Coping	−.188	−.010	−.047	.026	−.053	.082	.043	−.280*	.006	.054	−.030	−.010	.032	−.030
Relationships	−.108	−.030	.033	.020	.022	−.017	.066	−.185	−.029	.118	−.019	.052	−.064	.014
Self-worth	−.165	.097	.074	−.032	.154	−.147	−.061	−.044	.133	.112	.061	.015	.014	−.074
Psychosocial	−.222*	.081	.079	.126	.148	−.058	−.025	−.265*	.042	.132	.053	.083	−.012	−.054
Utility score	−.226*	.048	.016	.056	.126	−.104	−.028	−.240*	.123	.168	.062	.090	−.015	−.143

*$P < 0.05$.
**$P < 0.01$.
AA = arachidonic acid (omega-6); EPA = eicosapentaenoic acid (omega-3); DHA = docosahexaenoic acid (omega-3); n-6 = omega-6; n-3 = omega-3. Note that all change scores are calculated as 3 months minus baseline. Higher DASS scores = worse symptoms.
[a]Independent = independent living. Physical[b] = physical health. A higher AQoL score = better quality of life on that scale.

The improved mental health that was observed in both groups may in part be attributed to the social component of the study as both groups were exposed to group workshops (either cooking or social group). Furthermore, as all participants had depression there was an element of peer support in the group dynamic in both the social group and cooking workshops (where participants also share a meal together). Peer support, and particularly group-based peer support has been shown to be effective for treating depression, with equal efficacy to psychotherapy.[53] Nonetheless, there was evidence of greater improvement in the MedDiet group, consistent with population studies that have reported cross-sectional and longitudinal associations between poor diet and increased risk of depression, and conversely healthier diet and decreased risk.[13] This was supported in our study by multiple significant correlations between improved diet and mental health. The magnitude of benefit was large, with 60% fewer persons experiencing extremely severe levels of depression, 72% of anxiety and 69% of stress in the MedDiet group. The improved mental health in both groups is noteworthy, given that the Mediterranean diet is not just about healthy food – it is also about lifestyle, and this has been factored into the Mediterranean diet pyramid by including cultural and lifestyle elements such as conviviality and culinary activities.[10] Indeed, the cooking workshops we conducted previously with people who have serious mental illness were the most popular of all the workshops offered at Community Residential Care centres. As participants cooked and ate together, they progressively became more socially engaged as the workshops progressed.[28]

Nonetheless, there are also well-described biological mechanisms that support a causal underpinning to the observed relationship between diet and mental health. Dietary nutrients – including vitamins, minerals, polyunsaturated fats and amino acids – are essential for healthy brain structure and function. Nutrients are required as cofactors for hundreds of different enzymes; they support metabolic pathways, neurotransmitter synthesis, cell signalling, myelin sheath maintenance, glucose and lipid metabolism, mitochondrial function, prevention of oxidation and more.[54,55] Furthermore, factors that underpin poor physical health like inflammation, glucose intolerance, impaired cerebral blood flow and oxidative stress, also impact on mental health.[6,8,9,55,56] These factors are all related to poor diet.

This study is potentially limited by the fact that it was only single blinded, as participants could not be blinded to their treatment allocation. The measures and diet records are self-reported which cannot rule out expectation bias. Further, we recruited people with self-reported depression which may limit the generalizability to people with diagnosed depression – although there was no significant difference in severity of depression reported at baseline between those who were diagnosed or not. Drop out levels were relatively high, and more so in the social group, which may limit the generalizability of the results. We observed that many people dropped out from the social group because they had enrolled in the study in the hope of receiving dietary and cooking education, and expressed disappointment when advised of their group allocation after baseline assessments. Depression scores, gender, age, and income were not significantly different between those who completed 3-month assessments and those who dropped out. Strengths of the study include the study design; being a RCT; participants were instructed not to change any existing therapy or start any new therapy; and the 6-month follow up. Nonetheless, longer trials are needed to assess longer-term sustainability of the dietary changes and reduced depressive symptoms. We were able to correlate reported changes in diet/PUFAs and mental health outcomes to show that improvements were related to positive dietary and/or PUFA changes. Future studies with larger sample sizes could extend this with objective measures such as biological markers of improved dietary intake (e.g. carotenoids, urinary hydroxytyrosol) and underlying mechanisms for improved symptoms such as reduced inflammation, oxidation and increased brain-derived neurotrophic factor and correlating those with improved symptoms, as well as more robust inferential analyses (linear models for repeated measures adjusting for potential confounders). Importantly, we controlled for the social aspect of the cooking workshops (and research involvement more generally) to which people with depression can respond positively. Finally, statistical analysis included all cases, instead of being limited to cases with complete assessments over time.

This study supports preliminary findings from other dietary interventions that showed evidence of reduced depression in people with high CVD risk,[17] metabolic syndrome,[57] and unexpectedly in a trial of problem solving in elderly adults at risk for depression in the dietary arm that was used as a control.[58] Our study is one of the first RCTs to show benefits of healthier diet for mental health in a cohort of people with depression. Another Australian study was recently published, reporting improvements in depressive symptoms of people suffering major depressive disorder, and 32.3% achieving remission over 12 weeks.[59] In our study, the average depression score of the MedDiet group fell below the extremely severe depression cut-off, whereas in the social group it remained in the extremely severe range. Interestingly, while our study design was group based, the latter

intervention involved one-on-one dietetic counselling in the dietary arm and 'buddying' as a control arm, and had similar findings. More studies with larger sample sizes and objective markers are required.

Westernized societies have developed an alarming culture of increased takeaway and ultra-processed food consumption which not only has dire health consequences but has also removed people from enjoying the whole process of growing, cooking, and enjoying good wholesome food together. With the increased personal, societal and financial burden of chronic physical and mental illness, getting back to basics by promoting cooking skills and family/group meals could be such a simple yet powerful and empowering approach to healthcare and prevention.

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ORCID

Natalie Parletta http://orcid.org/0000-0003-2322-5555
Dorota Zarnowiecki http://orcid.org/0000-0003-0874-7830
Amy Wilson http://orcid.org/0000-0002-3855-0281
Svetlana Bogomolova http://orcid.org/0000-0003-4449-6514
Catherine Itsiopoulos http://orcid.org/0000-0003-1397-4149
Theo Niyonsenga http://orcid.org/0000-0002-6723-0316
Sarah Blunden http://orcid.org/0000-0002-5026-1992
Leonie Segal http://orcid.org/0000-0002-6391-6791
Bernhard Baune http://orcid.org/0000-0001-6548-426X

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