The effect of a Mediterranean diet on the symptoms of depression in young males (the "AMMEND: A Mediterranean Diet in MEN with Depression" study): a randomized controlled trial

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ABSTRACT

Background: Depression is a common mental health condition that affects 1 in 8 males each year, especially young adults. Young adulthood offers an opportunity for early dietary interventions, with research suggesting that a Mediterranean diet (MD) could be beneficial in treating depression.

Objectives: This study aimed to determine if an MD can improve depressive symptoms in young males with clinical depression.

Methods: A 12-wk, parallel-group, open-label, randomized controlled trial was conducted to assess the effect of an MD intervention in the treatment of moderate to severe depression in young males (18–25 y). Befriending therapy was chosen for the control group. Assessments were taken at baseline, week 6, and week 12. MD adherence was measured with the Mediterranean Diet Adherence Score (MEDAS). The primary outcome measure was the Beck Depression Inventory Scale—version II (BDI-II) and secondary outcome was quality of life (QoL).

Results: A total of 72 participants completed the study. After 12 wk, the MEDAS scores were significantly higher in the MD group compared with the befriending group (mean difference: 7.8; 95% CI: 7.23, 8.37; $P < 0.001$). The mean change in BDI-II score was significantly higher in the MD group compared with the befriending group at week 12 (mean difference: 14.4; 95% CI: 11.41, 17.39; $P < 0.001$). The mean change in QoL score was also significantly higher in the MD group compared with the befriending group at week 12 (mean difference: 12.7; 95% CI: 7.92, 17.48; $P < 0.001$).

Conclusions: Our results demonstrate that compared with befriending, an MD intervention leads to significant increases in MEDAS, decreases in BDI-II score, and increases in QoL scores. These results highlight the important role of nutrition for the treatment of depression and should inform advice given by clinicians to this specific demographic population. The trial was registered with Australia and New Zealand Clinical Trials Registry (trial ID ACTRN12619001545156) and has also been registered with the WHO International Clinical Trials Registry Platform (Universal Trial Number U1111-1242-5215). *Am J Clin Nutr* 2022;116:572–580.

Keywords: young adults, male, Mediterranean diet, major depressive disorder, quality of life

Introduction

Depression is a common mental health disorder affecting ∼350 million people worldwide (1). In Australia, ∼1 million Australian adults have depression in any given year, and early onset can mean that sufferers face varying degrees of disability for many years of their lives (2). Depression can present differently in each individual; however, the main characteristics include anhedonia, a depressed mood, and altered cognitive function (3). The overwhelming burden of mental illnesses affect young people, with the transition from adolescence through to adulthood presenting many challenges, such as significant transitions between home, educations, and employment (4).

From a developmental perspective, the ages 18–24 y have been described as emerging adulthood, which is a transitional developmental stage between late adolescence and adulthood (5). A sharp increase in depression rates are observed, with rates of mental illness peaking in emerging adulthood (6). Unfortunately, young males rarely seek help for their mental health, with only 13% of young males aged 15–24 seeking professional help (7). However, research shows that emerging adulthood also offers an opportunity for early lifestyle interventions, such as dietary change, because many are learning to cook and are taking control

This project was funded by Endeavour College of Natural Health and the University of Technology Sydney (UTS). It is an independent research project. The funding body had no involvement with the design, implementation, or analysis of the project.

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Abbreviations used: BDI-II, Beck Depression Inventory—version II; CONSORT, Consolidated Standards of Reporting Trials; CSIRO, Commonwealth Scientific and Industrial Research Organization; MD, Mediterranean diet; MDD, major depressive disorder; MEDAS, Mediterranean Diet Adherence Score; QoL, quality of life; RCT, randomized controlled trial; WHOQOL, World Health Organization Quality of Life Assessment.

Received December 16, 2021. Accepted for publication April 18, 2022.

First published online April 20, 2022; doi: https://doi.org/10.1093/ajcn/nqac106.

of their food choices for the first time (4). In addition, research consistently shows that males tend to display poorer diets when compared with women (8–10), making young males aged 18–25 with depression particularly in need of additional support.

Standard treatment of major depressive disorder includes psychotherapies such as cognitive behavioral therapy and antidepressant medications, such as selective serotonin reuptake inhibitors (11). However, ∼30% of depressed patients fail to adequately respond to antidepressant medications (12). Recently, researchers have been exploring the effect that specific nutrients (13–16), certain foods (17, 18), and various dietary patterns (19) have on mental health in the emerging field of nutritional psychiatry (20). Currently, the diet with the most evidence for exerting a positive effect on depressive symptoms is the Mediterranean diet (MD) (21).

The MD is high in fruits, vegetables, wholegrains, legumes, seafood, nuts, seeds, and olive oil, while being low in processed "fast" foods, red meat, and sugar (22). Although much observational evidence shows that those following an MD have a reduced risk of developing depression (23–26), only a few experimental trials have been conducted, showing that an MD can also help treat active major depressive disorder (MDD) (27, 28). However, these 2 trials have been performed in older adults, with a mean age of 40 (27) and 44 (28), with no studies to date exploring an MD in young adults with clinical depression. Interventions aimed at prevention or early treatment of depression are urgently needed.

Additionally, there is limited research on the effect of an MD on quality of life (QoL) in patients with depression, particularly young males. QoL questionnaires typically assess the participants' experiences of an illness, such as disability, fatigue, and pain, and can also include questions about participants' physical, social, and emotional well-being (29). Therefore, examining the impact of diet on QoL could provide additional insights into the efficacy of interventions across various domains of health (29).

Therefore, the aim of this research trial was to determine if nutritional counseling, focusing on the MD, could improve the diet quality, depressive symptoms, and QoL of young males with depression. We executed a randomized controlled trial (RCT) examining the effect of an MD compared with befriending therapy for the treatment of depression in young males with clinical depression. We hypothesized that following the MD would result in improved diet quality, depressive symptoms, and QoL in the MD group at week 12.

Methods

Study design

This was a 12-wk, parallel-group, open label RCT of an MD intervention in the treatment of moderate to severe depression. A detailed study protocol has been published elsewhere (30). The trial was registered with Australia and New Zealand Clinical Trials Registry (trial ID: ACTRN12619001545156) prior to commencing recruitment. It was also registered with the WHO International Clinical Trials Registry Platform (Universal Trial Number: U1111-1242-5215).

Participants were recruited from Australia over an 18-mo period. Participants were randomly assigned 1:1 to receive either dietary support or befriending (31). Participants in both groups completed assessments at baseline (week 0), midway (week 6), and at program completion (week 12). Ethics approval was received from the Human Research Ethics Committees of the University of Technology Sydney (UTS) on February 4, 2020: UTS HREC REF NO. ETH19-4413. Written informed consent was obtained from all participants after they had received a complete description of the study. The study's protocol was developed in accordance with the Standard Protocol Items: Recommendations for Interventional Trials guidelines (32). Primary and secondary outcomes were reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 guidelines and their extension to nonpharmacological treatments (33).

Patient and public involvement

During the development of the study protocol 10 young males with depression were invited to participate in a telehealth interview to give their opinion on the design of the trial, research questions, and outcomes measures. Modifications were then made to the study design to account for their priorities and preferences. At the conclusion of the trial, the results were disseminated to all trial participants via e-mail.

Study population and sampling

The study population consisted of young males aged 18–25 y who had been diagnosed with MDD by a general medical practitioner. Potential participants were recruited using targeted campaigns of flyers/posters, social media advertisements, databases from previous studies, and via a research participant recruitment company (Trialfacts, Melbourne, Australia).

Inclusion and exclusion criteria

The eligibility criteria included participants who were aged 18–25 y, identified as male, and had previously been diagnosed with depression by their medical doctor. They must also have scored ≥20 on the 21-item Beck Depression Inventory II (BDI-II), indicating moderate to severe depression, and have scored ≤40 on the Commonwealth Scientific and Industrial Research Organization (CSIRO) Diet Survey. The CSIRO Healthy Diet Score Survey asks questions about the quantity, quality, and variety of foods consumed. Individuals receive a personalized Diet Score out of 100 that reflects their overall compliance with the Australian Dietary Guidelines. A score of 75 has been proposed as a benchmark of a "good" score (34). A score of ≤40 on the CSIRO Diet Survey is considered poor. If participants were on antidepressant medications or undergoing psychotherapy, they were required to be on the same treatment for ≥2 wk prior to enrolment into the study. Participants were excluded if they had been diagnosed with any of the following disorders: bipolar disorder, posttraumatic stress, personality disorders, eating disorders, psychotic disorders such as schizophrenia, or a substance abuse disorder such as alcoholism. Participants were also excluded if they had any of the following that would prevent them from following the diet: gastrointestinal disorders such as Crohn disease, ulcerative colitis or irritable bowel syndrome; or food allergies, intolerances, or aversions (avoiding foods based

on religious or ethical grounds). In addition, participants were required to attend all appointments in order to complete the trial. Therefore, participants were excluded if they were unavailable to attend the scheduled follow-up appointments, were unwilling to change their diet if allocated to the MD group, or unwilling to participate in the befriending sessions.

Randomization

A computer-generated random number sequence was used in Microsoft Excel to randomly allocate participants using block randomization (block size 20). The Chief Investigator generated the sequence, and the Principal Investigator concealed the sequence in numbered sealed opaque envelopes. Participants were allocated a sequential number upon screening. The sealed envelopes corresponding to the allocated participant number were then opened at the baseline appointment by the researcher. The participant was then informed if they were randomly assigned to the MD intervention group or the befriending group.

Diet intervention group

The dietary intervention was delivered by a clinical nutritionist at the commencement of the trial during a 60-min appointment, which comprised personalized dietary advice, motivational interviewing, goal setting, and mindful eating to support optimal adherence to the MD. Participants also attended a 60-min follow-up appointment at weeks 6 and 12 that focused on additional goal setting, motivational interviewing, and overcoming any challenges they were facing following the MD. The MD used in this study was based on the dietary guidelines of Greece and Spain (35–37). The diet is rich in vegetables, legumes, wholegrains, oily fish, olive oil, and raw unsalted nuts. The primary focus is on increasing diet quality with fresh wholefoods while reducing intake of energy-dense, nutrient-poor "fast" foods. The following servings of food groups were recommended: wholegrains (5–8 servings/d), vegetables (5+ servings/d), fruit (2+ servings/d), legumes (1 serving/d), fish (2 servings/wk), nuts and seeds (1 serving/d), extra virgin olive oil (3 servings/d), dairy foods (1–2 servings/d), eggs (≤6/wk), poultry (2–3 servings/wk), red meat (1 serving/wk). Consumption of discretionary foods, such as sweets, fried food, processed meats, and sugary drinks, was limited to ≤3 servings/wk.

In addition to the 60-min nutritional counseling appointment, participants were also provided with a booklet containing information on serving sizes, sample meal plans, recipes, dining-out options, simple diet "swaps," eating-on-a-budget tips, compliance checklists, and an online daily diet history survey. Participants also received a food hamper valued at $50 at the commencement of the trial with a selection of Mediterranean foods. The diet was designed to be easy to follow, palatable, satiating, and aimed to fit within the participants' usual weekly food budget. Participants were advised that calorie restriction and weight loss were not an aim of the MD, and that they could consume permitted foods freely.

Control group

Participants allocated to the control group received befriending support sessions. These appointments followed the same visit schedule and duration as the diet intervention group. Befriending involves the researcher talking to the participant about neutral topics of interest such as movies, sports, and hobbies. The aim is to keep the participant engaged and interested. Befriending is an effective, credible, and acceptable validated control therapy for psychological studies and appropriate to participants suffering from mental illness (31). Befriending was chosen for its ability to control for some of the important factors that have been shown to confound RCTs. It controls for the client's expectations, the therapeutic relationship, and time spent with the nutritionist. Participants in the control group received a $50 Hoyts gift card at the program completion to thank them for their participation.

Data collection methods and instruments

Data were collected at baseline (week 0), midway (week 6), and project completion (week 12) using the following instruments: *1*) a case report form, which collected demographic data, medical history, and medications; *2*) the BDI-II 21-item, which measures depressive symptoms (38); *3*) the CSIRO Healthy Diet Score, which measures diet quality (39); and *4*) the World Health Organization Quality of Life Assessment (WHOQOL) form, which includes 26 questions on the individual's perceptions of their health and well-being over the previous 2 wk (40). Responses to questions were on a 1–5 Likert scale where 1 represents "disagree" or "not at all" and 5 represents "completely agree" or "extremely." The WHOQOL-BREF has been used in previous populations with MDD and has been shown to be a psychometrically valid and reliable instrument, appropriate for evaluating QoL in depressed patients (41). Four domain scores can also be derived from the QoL results. Domain scores are scaled in a positive direction, with higher scores denoting a higher QoL (40). The mean score of items within each domain is used to calculate the domain score. Mean scores are then multiplied by 4 to make domain scores comparable with the scores used in the WHOQOL-100 (40).

An adapted Mediterranean Diet Adherence Score (MEDAS) (39), which is a 15-item questionnaire assessing dietary habits considered characteristic of the Mediterranean diet in addition to assessing consumption of specific food groups, was also used. Each item is scored 1 or 0, depending on whether participants adhere to each MD component or not, and is summed for each individual providing a total score out of 15, with higher scores indicating greater adherence to the MD (39). In order to measure compliance and assess diet quality, participants documented all meals and snacks consumed during their time in the study via a widget on their mobile device. A detailed description of each can be found in the study protocol (30). The primary outcome measure was the BDI-II. This was used to assess depressive symptomatology at baseline and at the primary endpoint of 12 wk.

Sample size calculation

The sample size calculation was based on being able to detect a minimum clinically important change of >5 points in BDI (42) while comparing diet and placebo group, with $\alpha = 0.05$ and 80% power. In previous studies (43, 44) the response within each subject group was normally distributed with an approximate SD

of 7.5. Therefore, 36 participants were needed per group and 72 participants in total.

Data analysis methods

Statistical analysis was conducted using Stata (version 16; StataCorp LLC). The descriptive statistics reported included percentages, means, and SDs. The main outcome was the BDI-II score, which was analyzed as a continuous variable and reported as a mean. Assumptions for the repeated measures ANOVA were assessed and included the Bartlett test for homogeneity of variances. The Kolmogorov–Smirnov test for normality was also used to assess the distribution of the residuals in the data sets. Two-way repeated measures ANOVA was used to determine differences in BDI-II scores between each group across 3 time points, with time as the repeated measure. The Tukey honest significant difference (HSD) test was used to determine pairwise differences in mean BDI-II scores between the intervention and control group at week 6 and week 12. Two-way repeated measures ANOVA was also used to determine differences in MEDAS between each group across 3 time points, with time as the repeated measure. The Tukey HSD test was also used to determine pairwise differences in the MEDAS between the intervention and control groups at week 6 and week 12. Two-way repeated measures ANOVA was also used to determine differences in total QoL score between each group across 3 time points, with time as the repeated measure. The Tukey HSD test was also used to determine pairwise differences in total QoL scores between the intervention and control groups at week 6 and week 12**.**

Results

Baseline characteristics

A total of 165 participants were screened for eligibility, with 75 participants recruited into the trial between March 2020 and August 2021. Three participants (4%) withdrew from the study: 1 from the control group and 2 from the intervention group. All 3 withdrawals were due to commitment clashes meaning they were unable to attend appointments, and all withdrew within 48 h of enrolling. Therefore, their data were omitted from data analysis. A CONSORT flow chart outlining the study schedule and number of participants is displayed in **Figure 1**.

The mean age of participants was 22 y, and 71% ($n = 51$) of participants were born in Australia. A total of 45% ($n = 33$) of participants were seeing a psychologist, and 35% ($n = 26$) were taking medication for their depression, with 73% ($n = 19$) of those medications being selective serotonin reuptake inhibitors. Despite some participants receiving these therapies, all participants still had baseline depression scores indicating moderate to severe depression. The average time frame in which participants had been taking medications was 1 y, and the average time frame in which participants had been undergoing psychotherapy was 8 mo. A total of 30% ($n = 22$) used phone applications focused on mental health (Calm/headspace, etc.), and 75% ($n = 54$) had a family history of mental illness. The mean baseline depression score on the BDI-II scale was 34.8 for the MD group and 33.5 for the befriending group. All baseline measurements are reported in **Table 1**.

On average, the participants undertook 2 exercise sessions per week. When asked who is usually responsible for cooking and preparing their food and meals, 32% ($n = 23$) cooked their own meals, 43% ($n = 31$) had their meals prepared by someone else (parents/student accommodation/partner), and 25% ($n = 18$) relied entirely on fast food/take out. A total of 41% ($n = 31$) indicated that they had followed a specific diet in the past. The most frequently reported previous diet was intermittent fasting ($n = 9$). When asked to rate their overall sleep quality, 68% ($n = 51$) indicated poor sleep. When asked to rate their energy out of 10, the mean score was 4/10. When asked to rate their stress levels out of 10, the mean score was 6.

Outcome measure comparisons

The MEDAS was similar at baseline for both the MD and befriending groups. Significant within-group changes were observed at the 6-wk and 12-wk mark for the MD group but not the befriending group. The mean change between baseline and week 12 was 8.0 (95% CI: 7.41, 8.59) for the MD group and 0.2 (95% CI: −0.27, 0.67) for the befriending group. At week 12 the mean difference in MEDAS between the MD group and the befriending group was 7.8 (95% CI: 7.23, 8.37; $P < 0.001$). There were no side effects or adverse reactions from the MD reported. The results are displayed in **Table 2**.

The BDI-II scores were similar at baseline for both groups, and both groups saw a decrease in BDI-II scores. The mean change between baseline and week 12 was 20.6 (95% CI: 17.08, 24.33) for the MD group and 6.2 (95% CI: 1.83, 10.57) for the befriending group. The mean difference in BDI-II score between the MD group and the befriending group at week 12 was 14.4 (95% CI: 11.41, 17.39: $P < 0.001$). These results are displayed in **Table 3.**

At the conclusion of the study, 100% ($n = 36$) of participants in the MD group saw an improvement in their symptoms, with 36% ($n = 12$) of those participants reporting a final BDI-II score of 0–10, which indicates low or minimal depression. In the befriending group, none of the participants had a BDI-II score of 0–10 at the conclusion of the study.

For QoL, **Table 4** shows the statistical comparisons made between the MD and befriending groups, for the baseline and week 12 scores. Significant increases were observed in the MD group compared with the befriending group at week 12 for Domain 1—physical health ($P < 0.001$) and Domain 2—psychological health ($P < 0.001$). No significant differences between the MD and befriending group at week 12 were observed for Domain 3—social relationships ($P = 0.676$) and Domain 4—environment ($P = 0.512$). For the total QoL score, the mean change between baseline and week 12 was 18.3 (95% CI: 13.91, 22.69) for the MD group and 5.6 (95% CI: 0.26, 10.94) for the befriending group. The mean difference in total QoL score between the MD group and the befriending group at week 12 was 12.7 (95% CI: 7.92, 17.48; $P < 0.001$).

Discussion

In our cohort of young males with moderate to severe MDD, we hypothesized that nutritional counseling that focused on implementing an MD with a qualified nutritionist over 12 wk

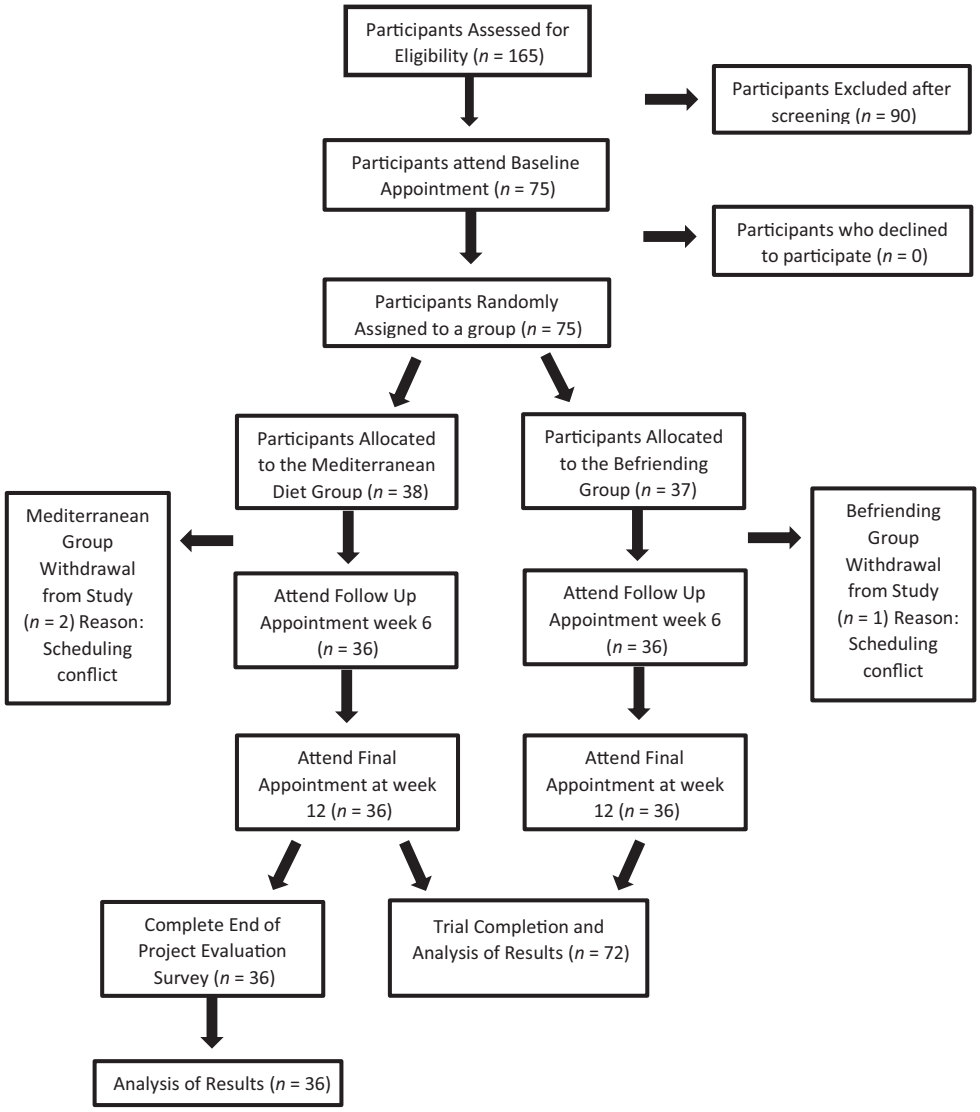

FIGURE 1 Consolidated Standards of Reporting Trials diagram for the AMMEND (A Mediterranean Diet in MEN with depression) trial.

would result in improved diet quality as measured by increases in the MEDAS in the MD group. We also hypothesized that improvements in diet from following an MD would result in reduced depressive symptoms, as measured by the BDI-II. In line with our hypothesis, our results demonstrate that nutritional counseling can effectively improve both the diets and depressive symptoms of young males with clinical depression after 12 wk of following an MD intervention.

We observed a mean reduction of 20.6 points on the depression scale for the MD group at 12 wk. We also observed 36% of participants in the MD group reporting low to minimal depressive symptoms at the completion of the trial. These findings build on the work of previous studies, which suggest a beneficial effect of diet on depressive symptoms in older adults (28, 45). Our results show that an MD can be effective in young males with moderate to severe clinical depression.

Dietary change comes with many challenges, and compliance over the long term poses significant difficulties for researchers, clinicians, and patients alike (46). Past research has also shown that males rate many health behaviors, including healthy food choices, as less important than women rate them (47), potentially leading to difficulties in engaging this demographic in dietary interventions. In addition, significant stigma around males following a "healthy diet" still exists in relation to hegemonic masculinity (48). Furthermore, fatigue and lack of motivation are common symptoms associated with depression and can pose additional challenges when making dietary changes.

However, a recent survey of young males with depression demonstrates that this demographic feel that their diet has a significant impact on their depressive symptoms and would be willing to change their diet in order to improve their mental health (49). The low dropout rate observed in our intervention group suggests high acceptability of the dietary intervention by the participants. The significant dietary improvements observed in the intervention group also demonstrate that dietary improvement is achievable for young males with clinical depression, regardless

TABLE 1 Demographic characteristics of study participants[1]

Item	MD group	Control group
Number of participants	36	36
Age (mean ± SD)	21.5 ± 2.9	22.5 ± 2.5
Born in Australia, *n* (%)	27 (75)	27 (75)
Habits		
Baseline CSIRO diet score/100 (mean ± SD)	35.1 ± 4.9	35.3 ± 4.7
Caffeine intake, drinks/wk (mean ± SD)	11 ± 8.2	9 ± 7.9
Alcohol intake, drinks/wk (mean ± SD)	6.6 ± 7.3	5.4 ± 5.3
Exercise sessions/wk (mean ± SD)	2.3 ± 2.1	2.5 ± 2.7
Cigarette smokers, *n* (%)	5 (13.8)	7 (19.4)
Recreational drug use, *n* (%)	12 (33.1)	13 (36.1)
Depression		
Baseline BDI-II score (mean ± SD)	34.8 ± 8.1	33.5 ± 9.0
Taking antidepressant medication, *n* (%)	11 (31)	15 (41)
Undergoing psychotherapy, *n* (%)	16 (44)	17 (47)
Using phone apps[2] focused on mental health, *n* (%)	11 (31)	11 (31)
Home		
Living at home with parents, *n* (%)	14 (39)	15 (42)
Living in student accommodation, *n* (%)	4 (11)	1 (3)
Share housing, *n* (%)	13 (36)	14 (39)
Living alone, *n* (%)	5 (14)	6 (17)
Money spent on food/wk, $A (mean ± SD)	110 ± 54.1	104 ± 56.7
Time spent cooking/day, min (mean ± SD)	44 ± 29.2	37 ± 30.7
Other factors		
Energy/10 (mean ± SD)	4.2 ± 1.5	4.0 ± 1.9
Stress/10 (mean ± SD)	6.5 ± 1.8	6.4 ± 1.8
Family history of mental illness, *n* (%)	26 (72)	28 (77)

[1] BDI-II, Beck Depression Inventory—version II; CSIRO, Commonwealth Scientific and Industrial Research Organization; MD, Mediterranean diet; $A, Australian dollars.
[2] Phone applications such as Calm, headspace, Smiling Mind, etc. which have a focus on mental health.

of potential diet stigma, and the challenging symptoms of their condition.

Our results also show that significant improvements in depressive symptoms can be seen over a short time period and these improvements can be sustained for the duration of the diet change. Previous research shows similar results, with a recent RCT demonstrating that following a healthier eating pattern for just 3 wk can lower self-reported depression symptoms in 17–35-y-old males and females (50). Additionally, our trial had fewer nutritional counseling appointments compared with the 2 previous RCTs, which assessed an MD in adults with depression—the SMILES study (45) and the HELFIMED study (28). Both RCTs incorporated 7 appointments over 12 wk, which is considerably more than the 3 appointments involved in our study. When designing the protocol for this trial, we invited young males with depression to give their opinion on the design of this RCT. As a result of this feedback, we chose to reduce the number of appointments to help with compliance and completion rates. Our results show that significant improvements in diet and depression can still be observed with less frequent appointments.

The mechanisms by which the MD might exert its beneficial effect on depression are complex and multifaceted (51). Numerous biological pathways appear to be involved affecting inflammation, oxidative stress, epigenetics, mitochondrial dysfunction, the gastrointestinal tract microbiome, tryptophan–kynurenine metabolism, the hypothalamic-pituitary axis, neurogenesis, and

TABLE 2 Comparison of MD and befriending groups using MEDAS[1]

Group	Baseline mean ± SD	Week 6 mean ± SD)	Week 12 mean ± SD	Baseline – week 12 mean change (95% CI)	Week 12 between-group mean difference (95% CI)	*P* value[2]
MD	3.3 ± 1.1	10.6 ± 1.3[3]	11.3 ± 1.4[4]	8.0 (7.41, 8.59)	7.8 (7.23, 8.37)	<0.001[5]
Befriending	3.3 ± 1.0	3.5 ± 1.0[3]	3.5 ± 1.0[4]	0.2 (−0.27, 0.67)		

[1] HSD, honest significant difference; MD, Mediterranean diet; MEDAS, Mediterranean Diet Adherence Score.
[2] *P* values are for 2-way repeated measures ANOVA.
[3] Tukey HSD for MD vs. befriending at week 6, $P = 0.001$.
[4] Tukey HSD for MD vs. befriending at week 12, $P = 0.001$.
[5] *P* value is <0.001 for the interaction of group, time, and group × time.

TABLE 3 Depression score (BDI-II) differences for MD compared with befriending[1]

Group	Baseline mean ± SD	Week 6 mean ± SD	Week 12 mean ± SD	Baseline − week 12 mean change (95% CI)	Week 12 between-group mean difference (95% CI)	*P* value[2]
MD	34.8 ± 8.1	19.8 ± 9.7[3]	14.1 ± 7.3[4]	20.6 (17.08, 24.33)	14.4 (11.41, 17.39)	<0.001[5]
Befriending	33.5 ± 9.0	29.7 ± 9.9[3]	27.3 ± 9.6[4]	6.2 (1.83, 10.57)		

[1]BDI-II, Beck Depression Inventory—version II; HSD, honest significant difference; MD, Mediterranean diet.
[2]*P* values are for 2-way repeated measures ANOVA.
[3]Tukey HSD for MD vs. befriending at week 6, $P = 0.001$.
[4]Tukey HSD for MD vs. befriending at week 12, $P = 0.001$.
[5]*P* value is <0.001 for the interaction of group, time, and group × time.

brain-derived neurotrophic factor (51). At present, depression is thought to arise from a combination of biological, psychological, and social factors (52). Whereas the benefits of nutritional psychiatry have primarily focused on the biological mechanisms (51), social and psychological benefits could also play an important role (53). Learning to prepare new foods and cooking with family and friends can also have a therapeutic effect (54).

Improvements to physical QoL were also reported in the MD group. These included improvements in concentration, sleep, and energy. Fatigue, poor sleep, and trouble concentrating are common physical symptoms of depression (55), therefore the improvements in depression could partially explain these findings. Additionally, individual components of the MD have been shown to affect each of these physical factors in previous research. Omega-3 fatty acids found in fish, and flavonoids found in fruits and vegetables show promise for improving cognitive function (56, 57), concentration, and memory (58). In addition, a low-fiber diet, high in sugar and saturated fat has been shown to impair sleep quality and is associated with lighter, less restorative sleep (59). Significant improvements in overall QoL were also reported in the MD group compared with the control. This suggests that following an MD can have a broader impact on young males with depression than expected, influencing many aspects of their health and well-being.

Although, to our knowledge, this is the first study to show that an MD can improve the symptoms of depression in young males with clinical depression, there are limitations to our trial that must be considered. Firstly, the short duration of this trial means we cannot determine the effect of long-term adherence to an MD and the effect this might have on depressive symptoms in young males with clinical depression. Secondly, due to ethical reasons we did not ask participants to suspend their depression medications or psychotherapy appointments. Despite some of the participants receiving these therapies, all participants still had baseline depression scores indicating moderate to severe depression. There were also no significant differences in the number of participants using these therapies between the MD group and the control group and as such we do not believe this

TABLE 4 WHOQOL-BREF total scores and domain scores for the MD and befriending group[1]

Group	Baseline mean ± SD	Week 6 mean ± SD	Week 12 mean ± SD	Baseline − week 12 mean change (95% CI)	Week 12 between-group mean difference (95% CI)	*P* value[2]
Domain 1: physical health[3]						
MD	49.3 ± 14.8	64.9 ± 12.8[a]	73.7 ± 10.5[b]	24.4 (18.37, 30.43)	17.7 (10.67, 24.74)	<0.001
Befriending	53.3 ± 15.4	57.6 ± 13.3[a]	59.9 ± 14.7[b]	6.6 (−0.48, 13.68)		
Domain 2: psychological[3]						
MD	32.0 ± 14.1	51.7 ± 16.4[c]	61.0 ± 13.6[d]	29.0 (22.49, 35.51)	22.1 (16.07, 28.13)	<0.001[4]
Befriending	35.7 ± 13.3	40.8 ± 13.4[c]	42.6 ± 15.3[d]	6.9 (0.16, 13.64)		
Domain 3: social relationships[3]						
MD	46.5 ± 18.8	52.9 ± 17.2	58.2 ± 15.2	11.7 (3.66, 19.74)	5.7 (−2.41, 13.81)	0.676
Befriending	45.9 ± 21.1	50.5 ± 21.5	51.9 ± 21.4	6.0 (−3.99, 15.99)		
Domain 4: environment[3]						
MD	67.5 ± 16.0	72.9 ± 12.4	77.0 ± 12.4	9.5 (−3.99, 15.99)	4.8 (−1.21, 10.81)	0.512
Befriending	66.8 ± 14.6	69.5 ± 13.8	71.5 ± 14.4	4.7 (−2.12, 11.52		
Total raw score						
MD	71.9 ± 10.1	83.7 ± 9.3[e]	90.2 ± 8.5[f]	18.3 (13.91, 22.69)	12.7 (7.92, 17.48)	<0.001[4]
Befriending	73.8 ± 10.8	77.5 ± 10.3[e]	79.4 ± 11.9[f]	5.6 (0.26, 10.94)		

[1]Means sharing a common superscript letter are significantly different at $P < 0.05$ (Tukey HSD). HSD, honest significant difference; MD, Mediterranean diet; WHOQOL-BREF,
[2]*P* values are for 2-way repeated measures ANOVA.
[3]Transformed scores (/100).
[4]*P* value is <0.001 for the interaction of group, time, and group × time.

to have significantly affected the results in any way. Per protocol analysis was used and thus the data from the 3 participants who withdrew from the study were not included in the final analysis.

Another potential limitation was the inability to blind participants to their treatment group, which could potentially affect the outcomes expected by participants. To combat this, the potential benefits of both diet and social support for mental health were presented as equal in their possible treatment efficacy, thereby reducing client expectancy bias. Additionally, information regarding the research hypothesis was withheld from the trial participants. Because the active control therapy of befriending has been shown to be somewhat effective for participants suffering from depression (60), we expected some improvement in this group. However, our results show that the MD is significantly more effective compared with befriending therapy.

In conclusion, this is to the best of our knowledge the first RCT to assess the impact of an MD on the symptoms of depression in young males with clinical depression. Considering the overall poor diet quality of depressed young males, coupled with the need for early interventions, this research provides a promising treatment option. Our results demonstrated that depressed young males can significantly change their diet quality over a short time period under the guidance of a clinical nutritionist. These dietary improvements led to significant improvements in depressive symptoms with no observed side effects. We also found that when compared with the control group, the MD group had significant increases in the physical and psychological health domains, as well as overall QoL. The results from this study can help guide future research in this area and inform advice given by clinicians to this specific demographic. Medical doctors and psychologists should consider referring depressed young men to a nutritionist or dietitian as an important component of treating clinical depression.

We thank Endeavour College of Natural Health and the Australian Research Centre in Complementary and Integrative Medicine (ARCCIM), University of Technology Sydney for providing funding for this research (Grant ID: 20200316-JB-1). JB acknowledges the support of the Australian Government Research Training Program Scholarship.

The authors' responsibilities were as follows—JB: conceptualized and designed the study; JS, DS: assisted with the development of the study design, methodology, and statistical analysis plan; JB: conducted research, was responsible for data collection, and performed the statistical analysis, which was reviewed by DS and JS; JB: drafted the manuscript with edits from JS and DS; and all authors: contributed to the manuscript and read and approved the final version. The authors report no conflicts of interest.

Data Availability

Data described in the manuscript, code book, and analytic code will be made available upon request pending approval.

References

1. Marcus M, Yasamy MT, van Ommeren Mv, Chisholm D, Saxena S. Depression: a global public health concern. American Psychological Association; 2012. doi.org/10.1037/e517532013-004.
2. Australian Bureau of Statistics. National survey of mental health and wellbeing: summary of results 2007. Canberra: ABS; 2008. Contract No.: 4326.0.
3. Schmidt HD, Shelton RC, Duman RS. Functional biomarkers of depression: diagnosis, treatment, and pathophysiology. Neuropsychopharmacology 2011;36(12):2375.
4. Collins S, Dash S, Allender S, Jacka F, Hoare E. Diet and mental health during emerging adulthood: a systematic review [Internet]. Emerg Adulthood 2020. doi:10.1177/2167696820943028.
5. Arnett JJ. Emerging adulthood: the winding road from the late teens through the twenties. Oxford University Press; 2014.
6. Aalto-Setälä T, Marttunen M, Tuulio-Henriksson A, Poikolainen K, Lönnqvist J. One-month prevalence of depression and other DSM-IV disorders among young adults. Psychol Med 2001;31(5):791–801.
7. Slade J, Teesson W, Burgess P. The mental health of Australians 2: report on the 2007 National Survey of Mental Health and Wellbeing. American Psychological Association; 2009.
8. Beer-Borst S, Hercberg S, Morabia A, Bernstein MS, Galan P, Galasso R, et al. Dietary patterns in six European populations: results from EURALIM, a collaborative European data harmonization and information campaign. Eur J Clin Nutr 2000;54(3):253–62.
9. Serdula MK, Gillespie C, Kettel-Khan L, Farris R, Seymour J, Denny C. Trends in fruit and vegetable consumption among adults in the United States: behavioral risk factor surveillance system, 1994–2000. Am J Public Health 2004;94(6):1014–18.
10. Davy SR, Benes BA, Driskell JA. Sex differences in dieting trends, eating habits, and nutrition beliefs of a group of midwestern college students. J Am Diet Assoc 2006;106(10):1673–7.
11. Amick HR, Gartlehner G, Gaynes BN, Forneris C, Asher GN, Morgan LC, et al. Comparative benefits and harms of second generation antidepressants and cognitive behavioral therapies in initial treatment of major depressive disorder: systematic review and meta-analysis. BMJ 2015;351:h6019.
12. Blier P, Ward HE, Tremblay P, Laberge L, Hébert C, Bergeron R. Combination of antidepressant medications from treatment initiation for major depressive disorder: a double-blind randomized study. Am J Psychiatry 2010;167(3):281–8.
13. Swardfager W, Herrmann N, Mazereeuw G, Goldberger K, Harimoto T, Lanctôt KL. Zinc in depression: a meta-analysis. Biol Psychiatry 2013;74(12):872–8.
14. Derom M-L, Sayón-Orea C, Martínez-Ortega JM, Martínez-González MA. Magnesium and depression: a systematic review. Nutr Neurosci 2013;16(5):191–206.
15. Almeida OP, Ford AH, Flicker L. Systematic review and meta-analysis of randomized placebo-controlled trials of folate and vitamin B12 for depression. Int Psychogeriatr 2015;27(5):727–37.
16. Bayes J, Schloss J, Sibbritt D. Effects of polyphenols in a Mediterranean diet on symptoms of depression: a systematic literature review. Adv Nutr 2020;11(3):602–15.
17. Saghafian F, Malmir H, Saneei P, Milajerdi A, Larijani B, Esmaillzadeh A. Fruit and vegetable consumption and risk of depression: accumulative evidence from an updated systematic review and meta-analysis of epidemiological studies. Br J Nutr 2018;119(10):1087–101.
18. LaChance LR, Ramsey D. Antidepressant foods: an evidence-based nutrient profiling system for depression. World J Psychiatry 2018;8(3):97.
19. Opie RS, O'Neil A, Itsiopoulos C, Jacka FN. The impact of whole-of-diet interventions on depression and anxiety: a systematic review of randomised controlled trials. Public Health Nutr 2015;18(11):2074–93.
20. Marx W, Moseley G, Berk M, Jacka F. Nutritional psychiatry: the present state of the evidence. Proc Nutr Soc 2017;76(4):427–36.
21. Altun A, Brown H, Szoeke C, Goodwill AM. The Mediterranean dietary pattern and depression risk: a systematic review. Neurol Psychiatry Brain Res 2019;33:1–10.
22. Martínez-González MÁ, Hershey MS, Zazpe I, Trichopoulou A. Transferability of the Mediterranean diet to non-Mediterranean countries. What is and what is not the Mediterranean diet. Nutrients 2017;9(11):1226.
23. Masana MF, Haro JM, Mariolis A, Piscopo S, Valacchi G, Bountziouka V, et al. Mediterranean diet and depression among older individuals: the multinational MEDIS study. Exp Gerontol 2018;110:67–72.
24. Skarupski KA, Tangney C, Li H, Evans D, Morris M. Mediterranean diet and depressive symptoms among older adults over time. J Nutr Health Aging 2013;17(5):441–5.
25. Yin W, Löf M, Chen R, Hultman CM, Fang F, Sandin S. Mediterranean diet and depression: a population-based cohort study. Int J Behav Nutr Phys Act 2021;18(1):1–10.

26. Fresán U, Bes-Rastrollo M, Segovia-Siapco G, Sanchez-Villegas A, Lahortiga F, de la Rosa P-A, et al. Does the MIND diet decrease depression risk? A comparison with Mediterranean diet in the SUN cohort. Eur J Nutr 2019;58(3):1271–82.
27. Jacka FN, O'Neil A, Opie R, Itsiopoulos C, Cotton S, Mohebbi M, et al. A randomised controlled trial of dietary improvement for adults with major depression (the "SMILES" trial). BMC Med 2017; 15(1):1.
28. Parletta N, Zarnowiecki D, Cho J, Wilson A, Bogomolova S, Villani A, et al. A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: a randomized controlled trial (HELFIMED). Nutr Neurosci 2019;22(7):474–87.
29. Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R. Quality of life measurement: bibliographic study of patient assessed health outcome measures. BMJ 2002;324(7351):1417.
30. Bayes J, Schloss J, Sibbritt D. A randomised control trial assessing the effect of a Mediterranean diet on the symptoms of depression in young men (the 'AMMEND' study): a study protocol. Br J Nutr 2021;126:730–7.
31. Bendall S, Jackson HJ, Killackey E, Allott K, Johnson T, Harrigan S, et al. The credibility and acceptability of befriending as a control therapy in a randomized controlled trial of cognitive behaviour therapy for acute first episode psychosis. Behav Cogn Psychother 2006;34(3):277.
32. Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med 2013;158(3):200–7.
33. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. Trials 2010;11(1):1–8.
34. Hendrie G, Baird D, Golley S, Noakes M. CSIRO healthy diet score 2016. Retrieved September 2016;10:2016.
35. Bach-Faig A, Berry EM, Lairon D, Reguant J, Trichopoulou A, Dernini S, et al. Mediterranean diet pyramid today. Science and cultural updates. Public Health Nutr 2011;14(12A):2274–84.
36. Food and Agriculture Organization of the United Nations. National nutrition guide for Greek adults [Internet]. Updated 2014 [cited Dec 12, 2021]. Available from: https://www.fao.org/nutrition/education/food-dietary-guidelines/regions/countries/greece/en/.
37. Food and Agriculture Organization of the United Nations. Food-based dietary guidelines - Spain [Internet]. 2008 [cited Dec 12, 2021]. Available from: https://www.fao.org/nutrition/education/food-dietary-guidelines/regions/countries/spain/en/.
38. Jackson-Koku G. Beck depression inventory. Occup Med (Lond) 2016;66(2):174–5.
39. Papadaki A, Johnson L, Toumpakari Z, England C, Rai M, Toms S, et al. Validation of the English version of the 14-item Mediterranean Diet Adherence Screener of the PREDIMED study, in people at high cardiovascular risk in the UK. Nutrients 2018;10(2):138.
40. Kim S. World Health Organization quality of life (WHOQOL) assessment. In: Maggino F, editor. Encyclopedia of quality of life and well-being research, 2nd ed. Springer; 2020. p. 1–2.
41. Berlim MT, Pavanello DP, Caldieraro MA, Fleck MP. Reliability and validity of the WHOQOL BREF in a sample of Brazilian outpatients with major depression. Qual Life Res 2005;14(2):561–4.
42. Masson SC, Tejani AM. Minimum clinically important differences identified for commonly used depression rating scales. J Clin Epidemiol 2013;66(7):805–7.
43. Tayama J, Ogawa S, Nakaya N, Sone T, Hamaguchi T, Takeoka A, et al. Omega-3 polyunsaturated fatty acids and psychological intervention for workers with mild to moderate depression: a double-blind randomized controlled trial. J Affect Disord 2019;245:364–70.
44. Sepehrmanesh Z, Kolahdooz F, Abedi F, Mazroii N, Assarian A, Asemi Z, et al. Vitamin D supplementation affects the Beck depression inventory, insulin resistance, and biomarkers of oxidative stress in patients with major depressive disorder: a randomized, controlled clinical trial. J Nutr 2016;146(2):243–8.
45. Jacka FN, O'Neil A, Opie R, Itsiopoulos C, Cotton S, Mohebbi M, et al. A randomised controlled trial of dietary improvement for adults with major depression (the "SMILES" trial). BMC Med 2017;15(1):23.
46. Crichton GE, Howe PR, Buckley JD, Coates AM, Murphy KJ, Bryan J. Long-term dietary intervention trials: critical issues and challenges. Trials 2012;13(1):1–10.
47. Wardle J, Haase AM, Steptoe A, Nillapun M, Jonwutiwes K, Bellisie F. Gender differences in food choice: the contribution of health beliefs and dieting. Ann Behav Med. 2004;27(2):107–16.
48. Gough B. 'Real men don't diet': an analysis of contemporary newspaper representations of men, food and health. Soc Sci Med 2007;64(2):326–37.
49. Bayes J, Schloss J, Sibbritt D. An investigation into the diets and nutritional knowledge of young men with depression (the "MENDDS" survey). Nutrition 2020;78:110946.
50. Francis HM, Stevenson RJ, Chambers JR, Gupta D, Newey B, Lim CK. A brief diet intervention can reduce symptoms of depression in young adults–a randomised controlled trial. PLoS One 2019;14(10):e0222768.
51. Marx W, Lane M, Hockey M, Aslam H, Berk M, Walder K, et al. Diet and depression: exploring the biological mechanisms of action. Mol Psychiatry 2021;26(1):134–50.
52. Garcia-Toro M, Aguirre I. Biopsychosocial model in depression revisited. Med Hypotheses 2007;68(3):683–91.
53. Chung C-F, Agapie E, Schroeder J, Mishra S, Fogarty J, Munson SA, editors. When personal tracking becomes social: examining the use of Instagram for healthy eating. In: Proceedings of the 2017 CHI Conference on human factors in computing systems; Denver, CO, May 6–11, 2017. New York (NY): Association for Computing Machinery; 2017.
54. Keller HH, Gibbs A, Wong S, Vanderkooy P, Hedley M. Men can cook! Development, implementation, and evaluation of a senior men's cooking group. J Nutr Elder 2004;24(1):71–87.
55. Kumar KS, Srivastava S, Paswan S, Dutta AS. Depression—symptoms, causes, medications and therapies. Pharma Innov 2012;1(3, Part A):37.
56. Castelli V, Grassi D, Bocale R, d'Angelo M, Antonosante A, Cimini A, et al. Diet and brain health: which role for polyphenols? Curr Pharm Des 2018;24(2):227–38.
57. Bauer I, Hughes M, Rowsell R, Cockerell R, Pipingas A, Crewther S, et al. Omega-3 supplementation improves cognition and modifies brain activation in young adults. Hum Psychopharmacol 2014;29(2):133–44.
58. Narendran R, Frankle WG, Mason NS, Muldoon MF, Moghaddam B. Improved working memory but no effect on striatal vesicular monoamine transporter type 2 after omega-3 polyunsaturated fatty acid supplementation. PLoS One 2012;7(10):e46832.
59. St-Onge M-P, Roberts A, Shechter A, Choudhury AR. Fiber and saturated fat are associated with sleep arousals and slow wave sleep. J Clin Sleep Med 2016;12(01):19–24.
60. Mead N, Lester H, Chew-Graham C, Gask L, Bower P. Effects of befriending on depressive symptoms and distress: systematic review and meta-analysis. Br J Psychiatry 2010;196(2):96–101.