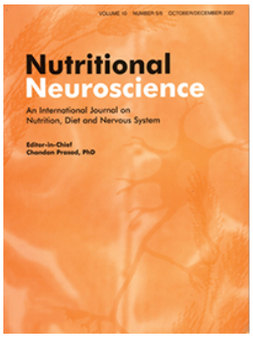

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Dietary recommendations for the prevention of depression

R.S. Opie[1,2], C. Itsiopoulos[1,2], N. Parletta[2,3], A. Sanchez-Villegas[2,4,5], T.N. Akbaraly[2,6,7,8,9], A. Ruusunen[2,10,11], F.N. Jacka[2,12,13,14,15]

[1]School of Allied Health, College of Science, Health and Engineering, La Trobe University, Melbourne, Australia, [2]International Society for Nutritional Psychiatry Research (ISNPR), Melbourne, Australia, [3]Sansom Institute of Health Research, Division of Health Sciences, University of South Australia, Adelaide, Australia, [4]Nutrition Research Group, Research Institute of Biomedical and Health Sciences, University of Las Palmas de Gran Canaria, Spain, [5]Ciber de Fisiopatología de la Obesidad y Nutrición (CIBER OBN), Instituto de Salud Carlos III, Madrid, Spain, [6]Inserm U 1198, Montpellier F-34000, France, [7]University Montpellier, France, [8]EPHE, Paris, France, [9]Department of Epidemiology and Public Health, University College London, UK, [10]Department of Psychiatry, Kuopio University Hospital, Finland, [11]Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland, [12]IMPACT Strategic Research Centre, Deakin University, Geelong, Australia, [13]Centre for Adolescent Health, Murdoch Children's Research Institute, Melbourne, Australia, [14]Department of Psychiatry, University of Melbourne, Parkville, Australia, [15]Black Dog Institute, Sydney, Australia

Background: Major depressive disorder is a common, chronic condition that imposes a substantial burden of disability globally. As current treatments are estimated to address only one-third of the disease burden of depressive disorders, there is a need for new approaches to prevent depression or to delay its progression. While in its early stages, converging evidence from laboratory, population research, and clinical trials now suggests that dietary patterns and specific dietary factors may influence the risk for depression. However, largely as a result of the recency of the nutritional psychiatry field, there are currently no dietary recommendations for depression.

Aim: The aim of this paper is to provide a set of practical dietary recommendations for the prevention of depression, based on the best available current evidence, in order to inform public health and clinical recommendations.

Results: Five key dietary recommendations for the prevention of depression emerged from current published evidence. These comprise: (1) follow 'traditional' dietary patterns, such as the Mediterranean, Norwegian, or Japanese diet; (2) increase consumption of fruits, vegetables, legumes, wholegrain cereals, nuts, and seeds; (3) include a high consumption of foods rich in omega-3 polyunsaturated fatty acids; (4) replace unhealthy foods with wholesome nutritious foods; (5) limit your intake of processed-foods, 'fast' foods, commercial bakery goods, and sweets.

Conclusion: Although there are a number of gaps in the scientific literature to date, existing evidence suggests that a combination of healthful dietary practices may reduce the risk of developing depression. It is imperative to remain mindful of any protective effects that are likely to come from the cumulative and synergic effect of nutrients that comprise the whole-diet, rather than from the effects of individual nutrients or single foods. As the body of evidence grows from controlled intervention studies on dietary patterns and depression, these recommendations should be modified accordingly.

Keywords: Prevention, Diet, Depression, Mental disorder

Introduction

Depression affects more than 350 million people worldwide, and, along with other mental health conditions, comprises the main contributor to global disability.[1] Depression also constitutes a major public health issue, as the burden of depressive disorders extends beyond disability to also influence mortality risk.[2] In terms of cost, depression is highly costly, accounting for 1% of the total economy of Europe (GDP).[3]

Major depressive disorder is a chronic condition, characterized by high rates of relapse and relatively low rates of remission.[4] As current treatments are estimated to address only one-third of the disease burden of depressive disorders,[5] there is a need for new

Correspondance to: Felice Jacka, Division of Nutritional Psychiatry Research, IMPACT Strategic Research Centre, Deakin University, PO Box 281, Geelong 3220, Australia. E-mail: f.jacka@deakin.edu.au

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approaches to prevent depression or to delay its progression. Converging evidence from laboratory, population research, and clinical trials suggests that healthy dietary patterns, such as the traditional Mediterranean-style whole-food diet, and specific dietary factors, including omega-3 polyunsaturated fatty acids (PUFAs), vitamin B6 and folate, antioxidants, and zinc, may influence the risk for depression.[6] Despite the consistency of published evidence on the relationship between dietary patterns and depressive disorders, arising from numerous observational studies carried out in recent years on large and heterogeneous populations (including diverse cultures and age groups),[7–9] and the emerging evidence suggesting that dietary improvement may prevent depression,[10,11] there are no dietary recommendations currently available regarding depression.

In line with a set of dietary and lifestyle guidelines for the prevention of Alzheimer's disease recently published by Barnard *et al.*,[12] we aimed to produce, in a similar format, specific dietary recommendations for the prevention of depressive symptoms and depression. In view of the global burden of depression, we believe it is timely to produce these recommendations, drawing on findings from published literature such as those highlighted in a recent viewpoint from an international collaboration of academics.[6] It is important to note that due to the recency of this new field of nutritional psychiatry, the existing data are largely drawn from observational studies and animal experiments, and there are few data from randomized controlled trials (RCTs) thus far.[13] In this sense, the current evidence can be considered only 'emerging' rather than established. However, given the substantial morbidity associated with depression, the high level of comorbidity of depression with diet-related physical disease, and the negligible risk of harm by promoting healthy diets, we believe it appropriate to invoke the 'precautionary principle' and propose a population health approach to prevention focused on dietary modification.[14] The aim of this paper is thus to provide a set of practical steps based on the best available evidence to inform public health and clinical recommendations.

Methods

Concordant with the dietary guidelines for prevention of Alzheimer's disease,[12] the following principles were applied to the development of these recommendations:

1. Dietary recommendations were based on substantial, although not necessarily conclusive evidence of benefit.
2. Implementation of dietary recommendations would present no reasonable risk of harm.
3. The recommendations will be subject to modification as scientific evidence evolves.
4. Individuals with comorbidities or dietary restrictions (e.g. food allergies) that prevent following general recommendations will need to tailor the recommendations to dietary choices that are safe and appropriate for their disease state.

Results

Five recommendations emerged from current published evidence and discussions with the authors, each of whom has substantial expertise in nutrition and psychiatry research. These are summarized as follows, and discussed in more detail below:

1. Follow 'traditional' dietary patterns, such as the Mediterranean, Norwegian, or Japanese diet. The available evidence suggests that traditional dietary habits may be beneficial for positive mental health.

2. Increase your consumption of fruits, vegetables, legumes, wholegrain cereals, nuts, and seeds. These foods should form the bulk of the diet as they are nutrient dense, high in fibre, and low in saturated and trans-fatty acids.

3. Include a high consumption of foods rich in omega-3 PUFAs. Fish is one of the main sources of omega-3 PUFAs, and higher fish consumption is associated with reduced depression risk.

4. Limit your intake of processed-foods, 'fast' foods, commercial bakery goods, and sweets. These foods are high in trans-fatty acids, saturated fat, refined carbohydrates, and added sugars, and are low in nutrients and fibre. Consumption of these foods has been associated with an increased risk or probability of depression in observational studies.

5. Replace unhealthy foods with wholesome nutritious foods. Healthy dietary patterns (e.g. fruits, vegetables, wholegrain cereals, and fish) and unhealthy dietary patterns (e.g. sweets, soft-drinks, fried food, refined cereals, and processed meats) are independent predictors of lower and higher depressive symptoms, respectively.

Discussion

The rationale for each of these recommendations is briefly discussed as follows.

Follow 'traditional' dietary patterns, such as the Mediterranean, Norwegian, or Japanese diets

Mediterranean, Norwegian, and Japanese dietary patterns are steeped in tradition – nutritionally and otherwise. Unique features include the predominance of whole-plant-based foods and fish, and the shared family and community experience in the consumption of these respective diets, including the ways in which dietary practices have been passed down from generation to generation. High adherence to these traditional dietary habits has been associated with reduced probability and/or risk for depression in observational studies.[8,15–18]

Global changes associated with urbanicity, the food supply, and food industry have resulted in profound shifts from traditional lifestyles and dietary patterns.[19]

A traditional whole-food diet provides an abundance of micronutrients, polyphenols, and healthy fats that are individually and collectively associated via multiple pathways with optimal brain function.[20] This includes critical roles in immune function, neuronal survival, energy metabolism, increased synthesis of neurotrophins and neurotransmitters, membrane fluidity, cell membrane integrity, glucose transport, nutrient synthesis and metabolism, gene expression, methylation, and reduced blood pressure, and neuroinflammation. Details of pathways associated with depression that could be modulated by diet are further discussed in Table 1.

Increase your consumption of fruits, vegetables, legumes, wholegrain cereals, nuts, and seeds

Evidence from recent meta-analyses found that diets higher in fruit, vegetables, wholegrain cereals, pulses, nuts, and seeds are associated with a reduced probability and/or risk for depression in observational studies.[7,8] However, much of the available evidence is cross-sectional in nature, which poses limitations in determining causality. Prospective cohort studies provide some evidence of the direction of the association, but RCTs help to clarify whether true causal associations exist between dietary patterns and depression. The PREDIMED trial, a large European multicentre RCT, showed that participants with Type 2 diabetes mellitus (T2DM) assigned to receive a Mediterranean diet supplemented with mixed nuts had a 41% reduction in the risk of developing depression compared with the control group ($P = 0.04$).[10] This Mediterranean diet comprised the following components: increased consumption of fruits, vegetables, legumes, and fish; 30 g/day of mixed nuts (15 g walnuts, 7.5 g hazelnuts, and 7.5 g almonds); abundant use of olive oil for cooking and dressing; reduction in total meat consumption, recommending white meat instead of red, or processed meat; preparation of homemade sauce with tomato, garlic, onion, and spices with olive oil to dress vegetables, pasta, rice, and other dishes; avoidance of butter, cream, fast-food, sweets, pastries, and sugar-sweetened beverages; and for alcohol drinkers – moderate consumption of red wine.[10]

These dietary factors potentially target low-grade systemic inflammation, endothelial, and metabolic disturbances, which are typically present in individuals with depression.[10] The high content of antioxidants in fruits and vegetables are likely to be protective,[7,21] because antioxidants defend against the negative effects of oxidative stress (such as neuronal damage), which has been associated with depression.[22] Berries, associated with reduced depressive symptoms as a part of a traditional Norwegian diet[17] and the healthy Finnish dietary patterns,[23] are also rich in polyphenols with antioxidant properties. Another explanation for the antioxidant–depression relationship is that polyphenols also have beneficial effects upon inflammatory markers (e.g. IL-6, CRP, and TNF-α), which are known to be elevated in depression.[24]

The potential protective effect of the whole-food diet could also come from nutrients such as folate, which is found in large amounts in some cruciferous vegetables (broccoli, cabbage, and Brussels sprouts), leafy vegetables (spinach and kale), other green vegetables (asparagus and avocado), citrus fruits, and dried legumes (lentil and chickpea).[21] A deficiency of folate has been reported in depressed populations,[6,20,25] while both low-dietary folate and low-folate status have been repeatedly shown to be associated with the probability of[26–28] and risk for depression.[29–31] Poor folate status has also been positively associated with severity of depression and with prolonged episodes of major depressive disorder.[25] Several mechanisms may link low-folate levels to depression risk, including decreased neurotransmitter synthesis, reduction in methylation reactions leading to lower *S*-adenosyl methionine and raised homocysteine levels, and direct effects on the central nervous system.[25] Moreover, low-dietary magnesium,[27,32] also found in vegetables, nuts, seeds, fish, legumes and whole grains, and hypomagnesemia[33] are both associated with depression.

Whole grains are abundant sources of dietary fibre, and the beneficial health effects may be partly mediated by its cereal fibre component. Cereal fibre intake is related to an improvement in insulin sensitivity and lipid profile, an increase in protective molecules such as adiponectin, and a reduction in inflammation markers.[34] Recent studies have shown significant and consistent protective effects of high intake of whole grains and cereal fibre on T2DM,[35] CVD,[36] and certain cancers.[37] Further, dietary fibres have specific and unique impacts on intestinal microbiota composition and metabolism, with recent studies relating gut microbiota to various chronic diseases.[34] Importantly, new evidence is emerging that suggests gut microbiota also influences mood and behaviour.[38]

Finally, plasma brain-derived neurotrophic factor (BDNF) levels are reduced in patients with depression,[39,40] whereas the Mediterranean dietary pattern supplemented with nuts is associated with increased plasma BDNF levels, especially among patients with depression.[41] BDNF is a peptide synthesized by neuronal tissue and vascular endothelial cells, and is critical for axonal growth, neuronal survival, and synaptic plasticity and function. Thus, the antioxidant, anti-inflammatory, and endothelial effects of the Mediterranean diet could explain the

Table 1 Dietary patterns and foods containing nutrients and health properties that may be protective or confer greater risk for depression

Food/nutrient	Association with depression risk	Dietary characteristics or components	Possible mechanisms
Mediterranean diet	(↓) Traditional dietary patterns, such as the Mediterranean diet, are beneficial for positive mental health[7,8,10]	The traditional Mediterranean diet is characterized by an abundance of plant-based foods (fruits, vegetables, wholegrain cereals, legumes, and nuts), olive oil as the principal source of fat, moderate consumption of fish, low-to-moderate intake of dairy products, and low intake of red meat	The Mediterranean diet has antioxidant, anti-inflammatory, and endothelial effects. This dietary pattern has also been shown to improve plasma BDNF levels
Other traditional whole-food diets	(↓) Traditional dietary patterns, such as the Japanese diet and Norwegian diet, are associated with decreased prevalence of depressive symptoms,[18] risk of suicide,[108] and positive mental health[17]	A healthy Japanese diet is represented by high intakes of vegetables, fruit, soy products, mushrooms, seaweed, fish, and green tea A traditional Norwegian dietary pattern consists of foods such as fish and shellfish, fruits, vegetables, and dairy products[17]	Health benefits likely related to combined effects of nutrients on mood. For example, the long chain omega-3 PUFAs found in fish, and antioxidants, such as those found in green tea, may have a role in decreasing the risk of mood disorders and suicide The diet pattern modulates immune and oxidative processes, and other biochemical parameters
Foods that are nutrient dense, high in fibre, and low in saturated and trans fats	(↓) May be associated with a reduced depression risk[7,8]	Fruits, vegetables, wholegrain cereals, legumes, nuts, and seeds	The high content of antioxidants in fruits and vegetables are likely to be protective. Potential protective effect of the whole-food diet could also come from folate and fibre
Fish and omega-3 fatty acids	(↓) A high fish consumption is associated with reduced depression risk[7,42,43]	Long chain omega-3 fatty acids are from marine sources, e.g. oily fish	Omega-3 fatty acids have vascular and anti-inflammatory properties, and are involved in enhancement of cell membrane fluidity and up-regulation of BDNF
Unhealthy dietary patterns	(↑) Higher consumption of energy-dense, nutrient-poor foods, and beverages are independent predictors of depression and other mental disorders[19,21,50]	Fast-food, commercial bakery goods, and sweets	Saturated fats may increase free radical production and promote pro-inflammatory states. Trans-fatty acids are associated with increased LDL-cholesterol, reductions in HDL-cholesterol, pro-inflammatory changes, and endothelial dysfunction. High-fat/sugar diets have negative impacts on brain plasticity in animal models.[109] High-GI foods are associated with adverse health effects and metabolic disturbances

positive association between the dietary pattern and BDNF levels.[41]

Include a high consumption of foods rich in omega-3 PUFAs

Fish is one of the main sources of omega-3 PUFAs, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and a high consumption of fish has been shown to be associated with reduced risk of depression.[7,42,43] As mentioned above, in people with depression, inflammation is increased and BDNF is reduced.[16] Whereas, omega-3 PUFAs can provide a range of neurochemical activities via the following mechanisms: modulation of neurotransmitter re-uptake, degradation, synthesis, and receptor binding; endothelial function and glucose transport across the blood–brain barrier; anti-inflammatory and anti-apoptotic effects; and the enhancement of cell membrane fluidity, and neurogenesis via up-regulation of BDNF.[6,20,21]

The National Heart Foundation of Australia[44] and the American Heart Association[45] recommend that people with documented Coronary Heart Disease (CHD) consume 1000 mg per day of combined DHA and EPA, e.g. through two to three serves (150 g per serve) of oily fish per week. Given the strong overlap of CVD with depression, this recommendation appears safe and appropriate. With respect to safe levels of fish consumption during pregnancy, all pregnant women are advised to consume 340 g per week (two 170 g servings) of low-mercury fish and seafood. This amount limits foetal exposure to trace amounts of neurotoxins (e.g. mercury and polychlorinated biphenyls).[46] Swordfish, king mackerel, shark (flake), and pike are high mercury-containing fish and should be avoided during pregnancy, whereas shrimp, salmon, sardines, and light tuna are safe options. Adequate consumption of omega-3 PUFAs is vitally important during pregnancy, as they are critical building blocks of foetal brain and retina. Pregnant women who consume little to no fish may be depriving the foetus of these essential nutrients.[46]

To date, there is some evidence that omega-3 supplementation via fish oil is beneficial for depression, despite large heterogeneity between studies.[47] Positive associations between fish consumption and depression may also be accounted for by the synergistic effects of macro- and micronutrients in fish.

Limit your intake of processed-foods, 'fast' foods, commercial bakery goods, and sweets

Recent prospective studies have demonstrated that a 'processed food pattern', e.g. high consumption of fast-food, commercial baked goods, and sweets, is associated with a higher probability or risk of depression.[21,48–50] The high content of trans-fatty acids in fast-food and commercial bakery products is likely one important contributor to the potential adverse effects of these dietary patterns. Trans-fatty acids are associated with increased plasma concentrations of LDL-cholesterol, reductions in HDL-cholesterol, pro-inflammatory changes, and endothelial dysfunction.[49] Such adverse biological modifications caused by trans-fatty acids may contribute to possible detrimental effects on depression.[49] Additionally, a 'processed food pattern' is typically high in saturated fat, which may increase free radical production and promote pro-inflammatory states, as well as promoting intestinal permeability,[51] which is also suggested as a relevant factor in depression.[52] Diets rich in saturated fatty acids or total fat have also been related to lower brain BDNF levels, lower neuronal plasticity, and poorer cognitive ability.[41] Moreover, while a recent preclinical study showed that a diet rich in sugar and fat or rich in sugar alone resulted in impairments in hippocampal-dependent memory, independent of weight changes, the sucrose-only diet was particularly associated with increases in hippocampal inflammation and oxidative stress.[53] There is also evidence to suggest that the impact on hippocampal functioning of a high-fructose diet may relate to increases in plasma triglycerides.[54]

While depression is associated with a chronic low-grade inflammatory response, higher levels of systemic inflammation may increase the risk for depression.[55] A potent source of inflammation is an unhealthy 'Western' dietary pattern, which has been shown to be associated with increased inflammatory markers and higher levels of CRP.[24] Such 'inflammatory' dietary patterns are also associated with depression risk.[56,57] Additionally, the 'Western' diet includes high-GI foods (e.g. refined cereal products and sugary foods) and represents a high-glycaemic load.[39] High-GI foods are associated with metabolic disturbances and increased oxidative stress. Increased levels of redox products, oxidative DNA damage, and telomere shortening are also features of major depression.[58]

Finally, omega-6 PUFAs, which predominate in vegetable oils, are abundant in the Western diet and are commonly found in commercial products like fast-food, as well as seed oils, and grain-fed animal products. Arachidonic acid, from the group of omega-6 PUFAs, is the principle precursor for the pro-inflammatory series of eicosanoids.[59] An imbalance of omega-6 and omega-3 PUFAs in the peripheral blood may cause an overproduction of pro-inflammatory cytokines, which are associated with the pathophysiology of major depression.[60]

Replace unhealthy foods with wholesome nutritious foods

Rapidly developing evidence from observational studies indicates that poor quality diets increase the

risk of depression and better quality diets act as a protective factor, and that these relationships are independent of each other. For example, in two large cohort studies of Australian adults, lower scores on the healthy dietary pattern and higher scores on a 'Western' unhealthy dietary pattern were independently associated with depression.[48,61] Similarly, the Whitehall II prospective cohort study found a protective association of an overall diet rich in fruits, vegetables, and fish, whereas a processed food pattern (rich in processed meat, chocolates, sweet desserts, fried food, refined cereals, and high-fat dairy products) was associated with an increased risk for depression incidence.[21,62] Importantly, data from population studies identifying healthy and unhealthy dietary patterns as predictors of depression suggest that healthy and unhealthy dietary patterns do not interact to jointly influence depression risk,[48,61] indicating that reduced intake of healthy foods may be a risk factor for depression, regardless of the intake of unhealthy foods, and vice versa.

In addition to the foregoing recommendations, other steps merit further investigation for possible inclusion in future iterations of prevention recommendations. These could include recommendations as follows.

Consume lean red meat in moderation

Earlier studies examining dietary patterns as predictors of illness have observed red meat to be a part of unhealthy dietary patterns,[63] and the traditional Mediterranean diet encourages the consumption of fish in place of red meats.[64] However, observational data suggest an association between limited or no meat consumption and poor mental health, although the direction of the relationship is unclear.[65,66] More recently, a cross-sectional analysis conducted in Australia reported that women consuming less (or more) than the recommended intake of red meat were more likely to have clinical depressive and/or anxiety disorders, as well as elevated psychiatric symptoms, than those consuming the recommended amount.[67] The level of red meat consumption associated with a reduced probability of these disorders was moderate at 28–57 g/day; equivalent to three to four serves per week (65–100 g per serve).[68]

The possible beneficial effects of consuming lean red meat in moderation might be attributed to the essential trace element zinc, as dietary zinc intake is inversely associated with depression.[27,69] Zinc deficiency is commonly observed in clinical depression[70] and has been linked to increased depressive symptoms.[71] Beef and lamb are among the richest sources of zinc.[72] Zinc has antioxidant properties, helps to maintain endocrine homeostasis and immune function, and plays multiple roles in regulating the hippocampal and cortical glutamatergic circuits that achieve affective regulation and cognitive function.[70] Thus, changes in zinc homeostasis might compromise neuroplasticity and contribute to long-term neuropsychological and psychiatric decline.[70]

Red meat is also an excellent source of bioavailable vitamin B12, hence, the possible mental health benefits from moderate red meat consumption may also be related to its vitamin B12 content. Folate and vitamin B12 are major determinants of one-carbon metabolism, in which *S*-adenosylmethionine (SAM)[58] is formed. SAM donates methyl groups that are crucial for neurological function. Low vitamin B12 levels have been shown to be associated with depressive disorders. Conversely, high vitamin B12 status may be associated with better treatment outcomes.[73]

Achieve an optimal vitamin D status

The importance of vitamin D to many brain processes including neuro-immunomodulation and neuroplasticity suggests that it might have a role in psychiatric illness such as depression.

Studies have shown an increased frequency of mood disorders and depression associated with low-serum concentrations of 25-hydroxyvitamin D (25[OH]D).[74–78] However, the data from RCTs are thus far equivocal and further research is needed to determine whether vitamin D can prevent and treat depression.[79]

With current food supplies and patterns of eating, it is almost impossible to obtain sufficient vitamin D from the diet alone. Thus, vitamin D status is generally maintained in the population by exposure to sunlight (or nutritional supplementation). Groups at the greatest risk of vitamin D deficiency are typically those with limited sun exposure, such as individuals who are housebound or in residential care as well as individuals with darker skin or who cover their skin for cultural or religious reasons.[80] The Australian and New Zealand adequate intake of 5.0 μg/day for younger adults (19–50 years) is based on the amount of vitamin D required to maintain serum 25[OH]D at a level of at least 27.5 nmol/l with minimal exposure to sunlight.[81] This points to the likely need for vitamin D_3 supplementation at an individual level or through vitamin D_3 fortification programmes at a population level to ensure adequate vitamin D status.

Include olive oil as the main source of added fat

Evidence indicates an inverse association between olive oil or oleic acid intake and depressive symptoms or depression risk.[49,82,83] Specifically, in the EPIC-Greece cohort study,[82] where the Geriatric Depression Scale score was inversely associated with dietary intake of olive oil, the mean olive oil intake

was 53.1 g/day for men and 47.0 g/day for females, which is substantially higher than the volumes typically consumed by non-Mediterranean populations.

The possible beneficial effect of olive oil on depression could be mediated through several mechanisms. Increased inflammation is frequently present in depressive patients,[24] and extra virgin olive oil contains bioactive polyphenols with important anti-inflammatory properties. The anti-inflammatory capacity of olive oil could improve the function of the endothelium. Moreover, the antioxidant actions of extra virgin olive oil components such as tyrosol are capable to restore the intracellular antioxidant defences decreased among depressive patients.[49] Olive oil may also be involved in important actions related to mood disorders through the synthesis of oleamide from oleic acid[49,84] – oleic acid represents more than 70% of olive oil. Oleamide has important actions related to mood disorders, such as the induction of sleep. It is also involved in the maintenance of the physico-chemical properties of membranes, thus improving the binding of serotonin to its receptors.[49,82]

Avoid alcohol abuse

Epidemiological data highlight the co-occurrence of depressive and alcohol use disorders.[85] While the temporal sequence of the occurrence of these two disorders is an area of contention,[86] evidence is growing to support the existence of a bi-directional association.[87–90] Prospective studies examining usual alcohol consumption, instead of alcohol disorders, on risk of depression provide mixed results. A Canadian study found no evidence for an association between level of alcohol consumption (any drinking, daily drinking, having more than one drink daily on average) and major depression. However, a trend in the data suggested that women who reported having more than five drinks on a maximal drinking occasion may be at increased risk of major depression.[91,92] Whereas, Spanish cohort studies show that low-to-moderate alcohol intake (5–15 g/day), and specifically wine consumption, is associated with lower risk of incident depression, compared to abstainers.[93,94]

A potential beneficial effect of moderate alcohol consumption – common in the traditional Mediterranean diet, in the form of red wine and, as a rule, during meals, has been reported for cardiovascular disease and mortality risk.[64] However, the hypothesis that 'moderate drinking is good for health' has been challenged by some authors who speculate that moderate drinking may actually be a sign of good health rather than a cause of it.[95] A recent exploration of the dynamic longitudinal relationship between mental health and alcohol consumption in the general population reported that mental health influenced changes in weekly alcohol consumption but not vice versa.[96] Additionally, two studies have shown that reports of drinking to self-medicate anxiety[97] or mood symptoms[90] was associated with increased incident alcohol dependence, as well persistence of dependence. Hence, anyone at risk of mental health conditions should discuss their alcohol intake with a health professional and avoid alcohol abuse.

Special groups – the adherence to these dietary recommendations could be especially important for individuals with cardiovascular disease, metabolic syndrome, or diabetes

Individuals with cardiovascular disease, metabolic syndrome, or T2DM are known to commonly suffer from, or be at risk of developing depression. There is some data to suggest that a healthy dietary pattern could be particularly useful to prevent depression among individuals with T2DM.[10,98] Depression is associated with worse prognosis in patients with coronary artery disease. And, major depression in acute coronary syndrome patients is associated with significantly lower plasma levels of omega-3 PUFAs (in particular of DHA), suggesting low omega-3 PUFAs as one common underlying mechanism.[99]

Additional comments

Current available evidence has been used to formulate these recommendations, which are designed to be a practical approach for supporting the health of populations. Although there is a current dearth of data from RCTs to demonstrate causality, such trials are inherently problematic given that – ideally – they require the long-term follow-up of large samples of participants following strictly controlled diets. Preliminary data from the large PREDIMED trial supports our recommendations,[10] despite being statistically underpowered to demonstrate true prevention of depression incidence. An RCT of dietary improvement as a treatment strategy for clinical depression is currently underway and may yield data supporting causality.[13] Similarly, a recent review of existing studies that have examined dietary interventions and mental health outcomes in non-depressed populations suggest some benefit, although the data are highly heterogeneous.[100] Nevertheless, while preliminary, at this point we believe that the current evidence from cross-sectional and prospective studies demonstrating clear and consistent associations between the probability or risk for depression across countries, cultures, and age groups,[7–9] as well as the extensive evidence from preclinical studies demonstrating the impact of dietary components on relevant physiological systems[101] is now sufficient to support such recommendations. This is particularly so given the extensive burden of disease

imposed by depression and the imperative to balance arguments regarding causality with an equal focus on developing interventions to improve population health.[102] Moreover, our recommendations are completely concordant with those for other, commonly comorbid, non-communicable diseases; thus the precautionary principle supports this approach.

Future considerations

Studies are now focusing on the epigenetic contributions to disease manifestation arising as a consequence of developmental programming. Epigenetic traits arising from poor early life nutrition have the potential to result in a population-wide manifestation of a phenotype (e.g. obesity, diabetes, and depression) over several generations.[103,104] Indeed, emerging evidence from large-scale cohort studies indicates a role for parental nutrition in mental health outcomes in children.[105–107] Understanding the role of early life nutrition and mechanisms of trans-generational epigenetic inheritance is essential for the development of future intervention strategies aimed at curbing the current chronic disease crisis.[103] Moreover, the rapidly developing research field focused on the gut microbiota is providing new and critical insights into key mechanistic pathways that, in turn, afford the development of targeted preventive and treatment interventions involving diet.[38]

Within feasibility constraints, methodologically rigorous RCTs will continue to be required to confirm causality in humans, with a particular focus on establishing ideal dietary recommendations at a macro- and micronutrient level. However, it is imperative to remain mindful that any protective effect of diet on depression is likely to come from the cumulative and synergic effect of nutrients from different sources of whole-foods, rather than from the effects of particular isolated nutrients or single foods. It is also critical to make the point that there is currently no data to suggest that dietary improvement could replace other forms of treatment for depression, including pharmacology and psychotherapy. Rather, dietary improvement should be considered as a strategy to support traditional treatments and improve overall health.

Conclusions

Although there are a number of important gaps in the scientific literature to date, existing evidence suggests that a combination of healthful dietary practices may reduce the risk of developing depression. These dietary recommendations may also provide additional and/or concurrent benefits for obesity, cardiovascular disease, T2DM and metabolic syndrome, and essentially pose no risk of harm. As the body of evidence grows from controlled intervention studies on dietary patterns and depression, these recommendations should be modified accordingly.

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Contributors All authors contributed equally.

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