

Can the Mediterranean diet decrease the risk of depression in older persons – a systematic review

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Summary

A significant proportion of the population aged 75 and over experiences an episode of major depression. Symptoms of depression manifested by elderly patients are sometimes treated as a natural element of the aging process, leaving elderly patients undiagnosed or misdiagnosed. It is postulated that the use of the Mediterranean diet may counteract the development of depression and alleviate depressive symptoms due to the anti-inflammatory properties of this diet. The aim of the systematic review was to assess whether the degree of adherence to the Mediterranean diet is related to the occurrence and severity of depressive symptoms in people over 65 years of age. We included 9 studies out of 317 identified manuscripts. The results of the studies included in the review indicate that adherence to the principles of the Mediterranean diet by elderly people may bring beneficial results in the prevention of depressive symptoms and justify further search for the relationship between this diet and its individual components with the mental well-being of elderly patients.

Key words: depression, Mediterranean diet, elderly

Introduction

According to the World Health Organization [1], depression is one of the leading causes of disability in the world. Its source is believed to be due to genetic, biological and environmental factors [2, 3]. Late-life depression refers to an episode of major depression that occurs after the age of 65, the frequency of which increases with age, affecting an average of 7.2% of people over the age of 75. In old age, multimorbidity and mortality increases, leading to a decrease in quality of life for older persons, and a subsequent increase in the need for health care services [2]. The key symptoms of depression include depressed mood, sleep disturbances, appetite disturbances, pessi-

mism, fatigue and agitation [4]. Symptoms of this type among the elderly are incorrectly treated as a normal element of aging, while it is estimated that over 70% of cases of depression in the elderly are undiagnosed or misdiagnosed [5].

Screening tests are used in hospitals to facilitate the identification of patients who display symptoms of depression. Popularly used self-report scales include the Hospital Anxiety and Depression Scale (HADS), the Center for Epidemiological Studies Depression Scale (CESD), Beck's Depression Inventory (BDI), and for the geriatric population the Geriatric Depression Scale (GDS).

The Mediterranean diet is a diet defined by observing the eating habits of people living in Crete, southern Italy, and the rest of the Mediterranean. The Mediterranean diet is characterized by a high supply of low-processed foods, such as fresh vegetables and fruits, grains, nuts, seeds and legumes, and a moderate supply of animal products: meat, eggs, and dairy. In this model of nutrition, fish is eaten twice a week, and olive oil is the main source of fat in the diet [6]. Due to the influence of this diet on the reduction of mortality due to cardiovascular disease, as observed in the Seven Countries Study, the Mediterranean diet has been subject to observational and clinical studies aimed at determining the effectiveness of its use in the treatment of specific disease entities [7]. It is postulated that the high intake of unsaturated fatty acids resulting from the composition of the diet with the simultaneous limitation of consumption of saturated fatty acids and trans fatty acids, as well as the intake of such dietary components as polyphenols, glutathione and selenium exerts a synergistic effect in alleviating the inflammation associated with cardiovascular disease, neoplasms and cognitive decline [8].

The pathophysiology of depression, including depression in older persons, is a complex issue, and some of the mechanisms underlying the development of this disease remain unclear [9]. An important role in the pathogenesis of affective disorders is probably played by the immune and inflammatory responses as well as disorders involving the production of free radicals [9, 10]. It is postulated that the Mediterranean diet may have a beneficial effect in the treatment of depression, which is attributed to the diet's individual components. One of the crucial components of the Mediterranean diet is olive oil, which is a source of EPA acid with proven anti-inflammatory and postulated neuroprotective effects [11]. The role of the antioxidant potential of the Mediterranean diet in the treatment of affective disorders is also indicated, as their pathogenesis is influenced by the disturbance of the brain functions due to the influence of free oxygen radicals [10]. Additionally, the results of studies conducted in a group of patients with depression showed that the persons with depression are characterized by a lower average level of folate than patients not suffering from the disease. Following the principles of the Mediterranean diet allows us to adequately meet the body's needs for group B vitamins, especially vitamins B6 and B12 and folates, involved in the methionine cycle, which is crucial for the proper metabolism of serotonin, dopamine, noradrenaline, and phospholipids of the central nervous system. Insufficient supply of group B vitamins in the diet may cause accumulation of homocysteine (hyperhomo-

cysteinemia) and disturbances in the production of neurotransmitters (monoamines), which are essential for maintaining a good mood [12, 13].

The aim of this systematic review is to assess, based on published reports, whether the degree of adherence to the Mediterranean diet is related to the occurrence and severity of depressive symptoms in the elderly.

Methods

The systematic review was conducted in accordance with PRISMA [14] recommendations according to the following search strategy: ((depress * [Title / Abstract]) AND (mediterranean [Title / Abstract])) AND ((elderly [Title / Abstract]) OR (olde * [Title / Abstract])). Keyword searches were performed in Medline-Ovid, Cochrane, Embase and PubMed databases resulting in 317 results. The procedure for selecting articles included in the review is shown in Figure 1. Duplicates and studies conducted before 2000 were excluded from the analysis. Only articles written in English were included in the review. The included studies investigate compliance with a Mediterranean diet among respondents over 65 years of age, which measured the severity of depressive symptoms using screening questionnaires to measure mood in the elderly and used the Food Frequency Questionnaire (FFQ) and the Mediterranean Diet Index (MDI) to assess compliance with a diet based on the Mediterranean standard. The abstracts of these studies were analyzed and excluded from further analysis due to: age of the respondents less than 65 years, no description of the method used to measure depressive symptoms among patients, and no description of dietary interventions or nutritional modifications that prevented it from being defined as a Mediterranean diet. As a result, nine studies were included in the systematic review.

Tools for measuring the severity of depressive symptoms

Only publications which precisely defined the method of measuring depressive symptoms among the respondents were included in the review. The GDS was used in six of the nine analyzed studies [15-20]. The CESD was used in two studies [7, 21] and the HADS in one of the studies included in the review [22].

Tools for the assessment of the diet of the subjects

One of the studies used only the Food Frequency Questionnaire (FFQ) [22] to assess dietary compliance with the Mediterranean diet pattern, two used only the Mediterranean Diet Score [16, 19], one used the Mediterranean Diet Questionnaire (MDQ) [15], and one used the Mediterranean Diet Adherence Score (MEDAS) [17]. Four studies included in the review used a combination of two tools, which in three of these were the Frequency of Consumption Questionnaire (whereby in one study was modified by the authors to include foods habitually consumed by Greek residents) and

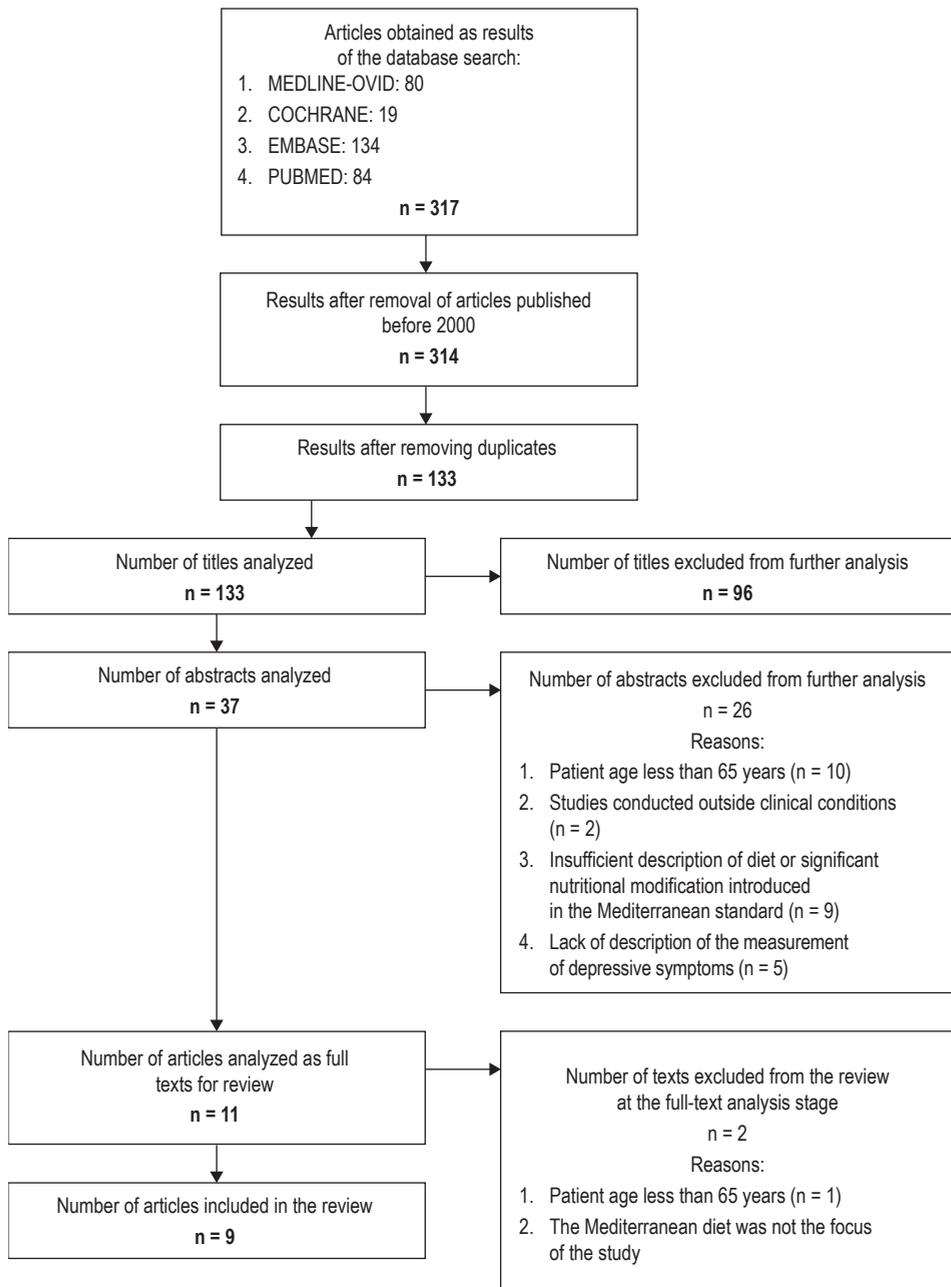


Figure 1. Procedure for selecting articles included in the review

the Mediterranean Diet Score [7], and in one study the EPIC-Greek Food Frequency Questionnaire and the Mediterranean Diet Score were used [18].

All studies included in the review were observational. Of the nine studies discussed, seven were conducted in Mediterranean countries [7, 15-20] where the Mediterranean diet is considered a traditional way of eating. The two other studies were conducted in the USA [21] and Scotland [22].

In eight studies, patients were aged 65 and over in the study group [7, 15, 17-22], and in one study the study group consisted of patients aged 90 to 99 years [16]. In six of the analyzed studies the participants were patients living in their own households [17-22], in two studies they were patients of a hospital or clinic operating at the hospital [7, 15], and one study included both patients living in their own households and those living in a nursing home [16]. In eight of the studies included in the review, patients underwent additional assessment including an evaluation of cognitive functions, nutritional status, as well as laboratory tests. The smallest group of respondents included 79 people [17], while the largest included 3502 people [21]. Two studies used a prospective assessment after 3 years [22] and after 30 days [7].

Comparator

The Health Aware Diet was only used in the study by Luciano et al. [22] as a comparator. The Health Aware Diet was characterized by the authors of the study as a fruit-rich nutrition model characterized by a low supply of meat products, eggs and alcohol.

Author, year	Country	Type of study / observation time	Number of subjects	Population	Additional tests and measurements	Method for measuring severity of depressive symptoms	Tool for measuring diet compliance with the Mediterranean model	Comparator	Results
Vicinanza et al., 2020 [15]	Italy	Cross-sectional study	143	Outpatients of geriatric care aged 65 and older (73.11 ± 8.35 years), independent in performing activities of daily living (ADL, IADL)	Sociodemographic data The burden of comorbidities using the CIRSG-SI scale, assessment of cognitive functioning using the MMSE questionnaire, assessment of physical activity using the PASE scale Laboratory tests: LDL, HDL, TG, total protein, ALT, AST	GDS	Mediterranean Diet Questionnaire	None used	Higher compliance with a diet based on the principles of the Mediterranean model is associated with a lower CIRSG-SI and GDS score and has an impact on the relationship between depressive symptoms and the rate of multimorbidity
Mantzorou et al., 2020 [19]	Greece	Cross-sectional study	2092	People aged 65 and over (74.97 ± 8.41 years)	Sociodemographic data BMI, MMSE, anthropometric measurements	GDS	Mediterranean Diet Score	None used	Higher compliance with the Mediterranean diet was related with less frequent concomitant depression (RR = 0.920, 95% CI (0.9-0.94), p<0.001)

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Pagiali et al., 2018 [16]	Italy	Cross-sectional study	388	Patients studied during home visits and nursing home patients, aged 90-99 years (92.7 ± 3.1)	Sociodemographic data ADL, IADL, MMSE, CDT, functional assessment measure	GDS	Mediterranean Diet Score	None used	Higher consumption of Mediterranean dietary elements such as olive oil and fruit was associated with a lower incidence of depressive symptoms. This relationship was statistically significant in women
Masana et al., 2018 [20]	International study: Cyprus, Malta, Italy, Spain, Greece, Turkey	Cross-sectional study	2718	Mediterranean island population aged 65 and over (74.2 ± 7.3) in the Mediterranean Islands Study (MEDIS)	Sociodemographic data BMI, anthropometric measurements Laboratory tests: glucose, triglycerides, LDL, HDL, total cholesterol	GDS	Food Frequency Questionnaire (FFQ), Mediterranean Diet Score	None used	Lower compliance with a diet based on the Mediterranean model seen in groups with moderate and severe depression
Hernández-Gallof et al., 2017 [17]	Spain	Cross-sectional study	79	People aged 65 and over (81 ± 4.6 years)	Sociodemographic data BMI, MMSE, questionnaire to measure physical activity, information on comorbidities, medications, smoking	GDS	Mediterranean Diet Adherence Score	None used	No correlation between the MEDAS score and the GDS

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Skarupski et al., 2013 [21]	USA, Illinois	Cross-sectional, prospective study with a follow-up assessment approximately every 3 years for 12 years	3502	People aged 65 and over	Sociodemographic data BMI, MMSE, evaluation of the speed of information processing with the use of the Symbol Digit Modalities Test, memory assessment using the East Boston Test of Immediate Memory and the East Boston Test of Delayed Memory questionnaires, ADL, IADL	CESD	Food Frequency Questionnaire (FFQ), Mediterranean Diet Score	None used	Higher dietary compliance with the Mediterranean diet was associated with a lower number of newly diagnosed depressive symptoms
Katsiardanis et al., 2013 [18]	Greece	Cross-sectional study	557	People aged 65 and over	Sociodemographic data Anthropometric measurements, information on current treatment, tobacco and alcohol usage Laboratory tests: LDL, HDL, triglycerides, total cholesterol, glucose Biochemical and hormonal determinations of fasting blood and saliva	GDS	The EPIC-Greek Food Frequency Questionnaire, Mediterranean Diet Score	None used	Mediterranean Diet Score was not associated with the GDS score (for men: $r = -0.1$, $p = 0.13$; for women: $r = -0.06$, $p = 0.3$)

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Luciano et al., 2012 [22]	Scotland	Cross-sectional study, follow-up assessment after 3 years	456	People aged over 65 (69.5 ± 0.8 years) at the first measurement and 72.5 (± 0.7 years) at the follow-up evaluation after 3 years, independent, with a low rate of multimorbidity	Sociodemographic data Laboratory tests: CRP, fibrinogen, albumin, IL-6, Tf, ferritin	HADS, questionnaire on the frequency of the appearance of depressive symptoms	Food Frequency Questionnaire (FFQ)	Health Aware Diet	The use of the Mediterranean diet was associated with a lower incidence of depressive symptoms. Such a relationship was not seen for the Health Aware Diet
Chrysohoou et al., 2011 [7]	Greece	Cross-sectional study, follow-up assessment after 30 days	277	People over 65 (75 ± 6 years), patients assessed up to 48 hours after admission, all diagnosed with coronary artery disease	Sociodemographic data Modified American College of Sports Medicine questionnaire to measure physical activity	CES-D validated for the Greek population	Food Frequency Questionnaire covering products and drinks habitually consumed in Greece, Mediterranean Diet Score	None used	A higher CES-D score was associated with a higher risk of a cardiovascular event within 30 days. When the MedDiet was included in the model, this association lost statistical significance, suggesting that diet compliance with the Mediterranean pattern is a modifying variable

BMI – Body Mass Index, ADL – Activities of Daily Living, IADL – Instrumental Activities of Daily Living, CIRSG-SI – Cumulative Illness Rating Scale – Geriatric, MMSE – Mini Mental State Examination, PASE – Physical Activity Scale for Elderly, GDS – Geriatric Depression Scale, TC – total cholesterol, HDL – high density lipoprotein, LDL – low density lipoprotein, TG – triglycerides, ALT – alanine transaminase, AST – aspartate transaminase, CDT – Clock Drawing Test, CRP – C-reactive protein, IL-6 – interleukin-6, Tf – transferrin.

Results

Among the nine articles from the Medline-Ovid, Cochrane, Embase and PubMed databases that met the criteria for inclusion in this review, the majority found a relationship between depressive symptoms and the use of the Mediterranean diet. In the study by Vicinanza et al. [15], the relationship between three elements was assessed: compliance with the Mediterranean diet model, patients' comorbidities and depressive symptoms. All three elements (GDS, MDQ, CIRSG-SI) of the proposed model correlated with each other (MDQ and GDS results: $r = -0.206$, $p = 0.014$; MDQ and CIRSG-SI results: $r = -0.251$, $p = 0.003$; GDS and CIRSG-SI: $r = 0.251$, $p = 0.003$), and adherence to the principles of the Mediterranean diet was associated with a decreased severity of depressive symptoms and lower incidence of multimorbidity. This study also showed that a one-point increase in the CIRSG-SI score was associated with a 1.33 point higher GDS score ($p = 0.028$). In the CIRSG-SI mediation analysis by MDQ, the GDS score increased by 0.38 points per 1 CIRSG-SI point ($p = 0.048$) [15].

Additionally, the study by Chrysohoou et al. [7] showed the modifying effects of compliance with a diet based on the Mediterranean model on the relationship between the severity of depressive symptoms and the risk of a cardiovascular event. The one-point increase in CES-D was associated with a 4% increase in the risk of a cardiovascular event. This relationship becomes less significant after the introduction of the Mediterranean Diet Score [7] to the model. The results of the other studies included in the review suggest that the use of the Mediterranean diet or the consumption of its specific elements (olive oil and fruit in the study by Pagliali et al. [16]) was associated with a lower frequency of diagnosed depressive symptoms. Such a relationship was also observed in the study by Luciano et al. [22] when comparing the Mediterranean diet with the Health Aware Diet. Contrary to the Health Aware Diet, better compliance with the Mediterranean diet was associated with lower inflammation and fewer depressive symptoms ($r = -0.13$, $p = 0.0001$) [22].

The observations on the relationship between the Mediterranean diet and the number of depressive symptoms are consistent with the results of other studies included in the review. The study by Masan et al. [20] showed that better adherence to the principles of the Mediterranean diet was associated with a 35% reduction in the risk of depressive symptoms (OR: 0.65; 95%CI: 0.50-0.85). The results of the study by Skarupski et al. [21] show the relationship between the occurrence of depressive symptoms and the compliance with the Mediterranean diet model such that each 5-point increase in the Mediterranean Diet Score was associated with a decrease in the rate of increase in depressive symptoms from 7.4% to 6.4% per annum. The group with the lowest adherence to the Mediterranean diet model showed the highest rate of depressive symptoms.

A significant relationship between the use of the Mediterranean diet and depressive symptoms was found in the study by Mantzorou et al. [19] where participants whose diets deviated from the Mediterranean pattern obtained a higher GDS score than those participants who showed high compliance of their diet with the described

model. However, a statistically significant relationship between the application of the principles of the Mediterranean diet and the appearance of depressive symptoms was not found in the study by Katsiardanis et al [18].

Discussion

Most of the studies described in the review concluded that following the Mediterranean diet was associated with a lower incidence of depressive symptoms. The Mediterranean diet, due to its high content of antioxidants and anti-inflammatory ingredients, is considered the healthiest diet and is one of the most studied nutritional models [23]. Links are being sought for a high degree of compliance with the diet of the Mediterranean model with the reduction of the risk of cardiovascular diseases, reduction of inflammation associated with metabolic diseases, and the incidence of cancer [23, 24]. One of the directions of research on the described diet is its use in the treatment of people suffering from cognitive and depressive disorders. Research by Feart et al. has shown that better adherence to the recommendations of the Mediterranean diet is associated with a slower decline in the results obtained by patients when performing the MMSE (Mini Mental State Examination) in subsequent years, which, due to the correlation of cognitive disorders with depression shown by other authors may set the direction for further research looking for a relationship between nutrition and the occurrence of late-onset depression [25-27]. Additionally, people following the principles of the Mediterranean diet have a lower average BMI, which is associated with a lower risk of depression than in those who are underweight, overweight, and obese [28, 29]. Therefore, in the population of geriatric patients, equal importance should be placed on counteracting malnutrition as on optimal weight reduction in overweight and obese people. Mental well-being may also be influenced by less frequently discussed factors, such as glucose tolerance or blood flow in the brain, which are also related to the quality of the consumed diet and the dietary content of individual elements and vitamins [30].

The 2015 PREDIMED study [31] in Spain, which aimed to assess the long-term effects of the Mediterranean diet, also provided data on the relationship of such a model of nutrition with the development of depression in the group of people aged 55 and over. This study was not included in this review due to the adopted age criterion, but the results obtained by the authors constitute an important contribution to the discussion on the relationship between the Mediterranean diet and depressive disorders. The analysis included 3923 participants aged 55-80 (for men) and 60-80 (for women). Participants in the PREDIMED study were randomly assigned to one of three groups: the Mediterranean diet enriched with olive oil, the Mediterranean diet with the addition of a nut mix, and the control group eating a low-fat diet as recommended by the American Heart Association. In the group of people included in the analysis devoted to the relationship of the Mediterranean diet and depression, 224 new cases of depressive disorders, understood as a diagnosis made by a doctor and reported by the participant during any of the interviews during the study, or the participant reporting the use of antidepressants

sants, were noted. No relationship was found in the study between the introduction of the Mediterranean diet and the risk of developing depression. In the group where the participants consumed the Mediterranean diet with the addition of a nut mix, a nearly 30% reduction in the risk of developing depression was noticed, but the difference was not statistically significant. When the same analysis was performed with participants only with type 2 diabetes, the group of patients assigned to the Mediterranean diet with nuts had an average 41% lower risk of developing depressive disorders than members of the control group [31]. The results of this study differ from those obtained in the studies included in the review. The results obtained in the PREDIMED study and the studies included in the review provide observations justifying further research in this area, although they do not allow for a clear conclusion that the Mediterranean diet is associated with a lower risk of developing depressive disorders in the elderly population.

The results of the meta-analysis by Psautopoulou et al. [32], taking into account studies involving younger participants, confirm that the high compliance of the diet based on the Mediterranean model reduces the risk of developing depression, regardless of age. An average level of compliance of the nutritional model with the Mediterranean diet also reduces the risk of developing depression, but this positive effect diminishes with age. In order to fully assess the effectiveness of the Mediterranean diet in the prevention and alleviation of depressive symptoms, it should be compared with other popular and fully-fledged nutritional models, such as the MIND diet (Mediterranean-DASH Intervention for Neurodegenerative Delay) or the DASH diet (Dietary Approach to Stop Hypertension). Fresán et al. [33], while studying the participants of the SUN (Seguimiento University of Navarra) cohort in 2014 and 2016, found that while the use of the Mediterranean diet is associated with a lower risk of developing depression, no statistically significant correlation is observed for the MIND diet. This is an interesting observation because this diet was designed to prevent cognitive decline as a combination of the DASH diet and the Mediterranean diet [34, 35]. A study conducted by Perez-Cornago and his team [36] showed a correlation between the use of the DASH diet and a reduced risk of developing depression. Such a relationship was only observed when the researchers measured the compliance of the diet with the DASH diet pattern using the Fung and Mellen indices. No such relationship was observed for the other two indices used to evaluate the DASH diet (Dixon, Günther). This study also did not address the Mediterranean diet for the purpose of comparing the two nutritional models. Both of these studies, conducted by Fresán et al. and Perez-Cornago et al., included a group of adults, without including a separate group of elderly patients. Meanwhile, the results of the studies included in the review indicate that adherence to the principles of the Mediterranean diet by elderly people may bring beneficial results in the prevention of depressive symptoms and justify further search for the relationship between this diet and its individual components with the mental well-being of elderly patients.

When conducting research in the above-mentioned population, it is necessary to take into account the deterioration of cognitive functioning with age, including memory

and errors that may therefore occur when collecting nutritional history. It should also be remembered that memory disorders in the group of elderly patients often coexist with depression [37].

When planning a nutritional intervention, one should consider the deteriorating ability to adapt with age, including a reduced ability to accept new tastes or products in the daily menu [38]. It seems reasonable to recommend that in the case of introducing the Mediterranean diet, one should rely on already known products, combine them with new products and gradually adjust the supply of all ingredients to the actual needs of the patient. Products that are present in the menu of the Mediterranean diet but are also commonly used in the cuisine of Poles, include whole grain cereal products, olive oil, legumes, tomatoes, garlic, and onions. The pursuit of the greatest possible compliance of a given diet with the Mediterranean diet model while considering the individual's preferences to achieve better adherence to the recommendations should be seen as a beneficial intervention at every stage of life. The high content of anti-inflammatory, antioxidant and neuroprotective ingredients justifies the hypothesis about the antidepressant potential of the Mediterranean diet in the population of older persons and prompts further research in this area.

Conclusion

The conducted review does not allow for clear confirmation that the introduction of the Mediterranean diet will contribute to the reduction of the risk of depression among geriatric patients. The studies included in the review were mainly cross-sectional in nature and were also conducted with the use of various research procedures, different tools for the assessment of depressive symptoms and the principles of assessing the Mediterranean diet. However, the results of the presented studies provide evidence that the implementation of the Mediterranean diet or its elements may be a useful nutritional intervention among patients over 65 years of age, not only because of the cardiovascular risk. Further studies are needed to confirm the relationship between depressive symptoms and compliance with the Mediterranean nutritional model in this patient group.

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