ASSOCIATION OF LONG-TERM MEDITERRANEAN DIETARY PATTERN AND DEPRESSIVE MOOD IN OLDER ADULTS: A SYSTEMATIC REVIEW OF COHORT STUDIES

Christina Jeanny Soekiono[1*], Sherlyn Sean[1]

[*]Corresponding author email: christinajeannysoekiono@gmail.com

DOI: https://doi.org/10.33508/jwmj.v6i4.5993

ABSTRACT

Introduction: Depression is a significant global health concern that occurs frequently among individuals aged 65 and older. In addition to pharmacological therapy and psychotherapy, dietary interventions play a crucial role in the multifactorial, biopsychosocial treatment of psychiatric disorders and could be used as a potential therapeutic target. Increasing evidence is emerging about the important role of the Mediterranean diet (MeDi) in the pathophysiology of mood disorders, particularly depression. **Objective:** This systematic review aims to assess whether long-term adherence to MeDi affects depressive symptoms in the elderly based on published cohort studies. **Method:** Literature searches are conducted on several databases (PubMed, ProQuest, ScienceDirect, and Google Scholar) with keywords related to "Mediterranean diet", "depression" and "elderly". **Result:** The research was done based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol. Studies were then screened based on the inclusion criteria, with the result of 3 included cohort studies out of 5,123 identified studies. Study characteristics were extracted and the risk of bias was assessed with the Joanna Briggs Institute Critical Appraisal Checklist for each study. **Conclusion:** Based on the study analysis, the relationship between adherence to the Mediterranean diet and depression in elderly over time is inconclusive due to conflicting results and limited studies.

Keywords: Mediterranean diet, depression, elderly

[1] *School of Medicine & Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta,*

INTRODUCTION

Depression is a significant global health concern, affecting people of all ages and backgrounds. According to the World Health Organization (WHO), around 280 million people in the world have depression.[1] Late-life depression refers to an episode of major depression occurring in individuals aged 65 and older, with an expected prevalence of 31.8%. The actual number is likely even higher because depression symptoms are sometimes treated as a natural element of the aging process, leaving the elderly undiagnosed or misdiagnosed. This results in an overall economic burden, including health service utilization.[2] Common manifestations of depression in elderly include depressed mood, loss of interest or pleasure in daily activities, pessimism, physical discomfort symptoms, loss of appetite and weight, and sleep disturbances.[3]

In addition to pharmacological therapy and psychotherapy, dietary interventions play a crucial role in the multifactorial, biopsychosocial treatment of psychiatric disorders and could be used as a potential therapeutic target. Various mechanisms were identified through which diet and its components may affect the modulation of the pathways involved in inflammation, oxidative stress, mitochondrial dysfunction, gut microbiota, the hypothalamic-pituitary-adrenal (HPA) axis, and neurogenesis.[4]

Increasing evidence is emerging about the important role of the Mediterranean diet (MeDi) in the pathophysiology of mood disorders, particularly depression. The disruption of the HPA axis in depressed patients, which results in elevated cortisol levels, can be addressed by consuming a Mediterranean diet rich in polyphenols, known for its cortisol-lowering effects.[5] Olive oil, the main source of fat in this diet, contains eicosapentaenoic (EPA) acid that has anti-inflammatory and neuroprotective properties, which may reduce inflammatory markers, including plasma C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor-α (TNF-α).[6] Moreover, MeDi has also been linked with decreased oxidative stress biomarkers and enhanced neuroplasticity.[7] Essential vitamins and minerals crucial in the metabolism of serotonin, dopamine, noradrenaline, and phospholipids of the central nervous system, also play a significant role in maintaining a positive mood.[8]

A systematic review of cross-sectional studies on this subject found that implementing the MeDi or its components may be a useful nutritional intervention for patients over 65 years of age. However,

there is still no definitive evidence to confirm a causal relationship.[9] Therefore, this systematic review aims to assess whether long-term adherence to the MeDi is affecting the depressive symptoms in the elderly based on published cohort studies.

METHOD

Literature searches

Literature searches were conducted with the database PubMed, ProQuest, ScienceDirect, and Google Scholar on the date June 28, 2024, for articles associated with the adherence to the Mediterranean diet on depression in the elderly. Database searches are done with the keywords "Mediterranean diet", "depression", "elderly" and their synonyms. The inclusion criteria of the studies are cohort studies with a population aged ≥65 years old at baseline; studies published in the last 10 years; and publications in either Indonesian or English.

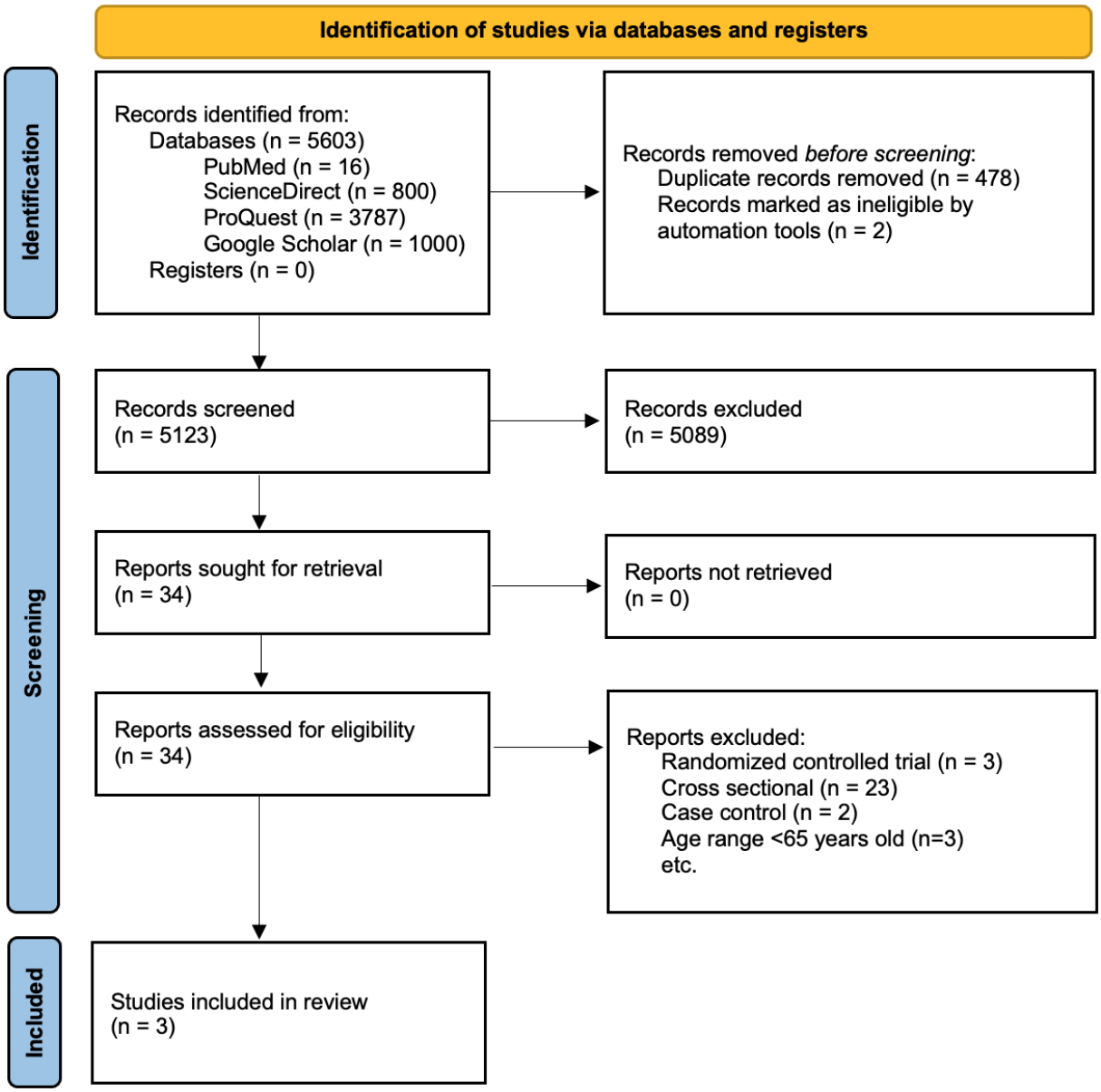
Screening, data extraction and risk of bias assessment

Studies that were found with the literature searches from each database were then exported to Zotero 6.0.37. Duplicates and retracted articles were excluded, and screening was done based on the title and abstract of the studies relevance to the topic on adherence to the MeDi and depression in older adults. For studies where relevance could not be determined from the abstract and title, the full text was reviewed. Population age, country, number of participants, duration of follow-up, depression and MeDi adherence scoring, and covariates adjusted model were then extracted from the screened studies. The risk of bias for each included study was independently evaluated by two reviewers with the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Cohort Studies to assess the quality and identify any potential biases.[10] Any disagreements between the reviewers were resolved through consensus.

RESULT

This research was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol.[11] The selection of studies was carried out according to the PRISMA diagram shown in Figure 1.

Figure 1. PRISMA Diagram



Three included cohort studies were selected by the inclusion criteria, with each study's characteristics outlined in Table 1. Two of the studies (50%) are conducted in Mediterranean countries, with the population aged ≥65 years old. The risk of bias in each study is assessed based on the JBI Critical Appraisal Checklist for Cohort Studies[10], with results summarized in Table 2.

Table 1. Study characteristics

(Author, Year); Country	Population (Number of participants)	Duration of Follow-up	Depression Scoring	MeDi Adherence Scoring	Covariates Adjusted Model	Results
(Mamalaki *et al.* 2023)[12]; Greece	Aged ≥65 y.o; mean age of 73.3 ± 5.0 y.o (n=879)	Mean = 3.0±0.8 years	GDS	MedDietScore	**Basic Model:** adjusted for age, sex, and years of education **Model 1:** Basic model excluding participants with dementia at baseline **Model 2:** Basic model excluding participants with dementia and MCI at baseline **Model 3:** Model 2 + controlling for Baseline Global Cognition Score **Supplementary Model:** age, sex, years of education, if the participant lived alone, number of comorbidities, smoking status, physical activity and BMI	Negatively associated with depression incidence (based on basic model; p<0.001)
(Bardinet et al., 2022)[13]; France	Aged ≥65 y.o; mean age of 75.6 ± 4.8 y.o (n=1018)	Median = 11.5 years	CES-D scale	MeDi-Lite score, MDS, and MedDietScore	**Baseline value:** adjusted for age, sex, educational level, living conditions, physical activity, tobacco consumption, BMI, total energy intake and multimorbidity	Not associated (based on baseline value; p=0.404)
(Cherian *et al.* 2020)[14]; USA	Mean age of 80.4 ± 7.2 y.o (n=709)	Mean = 6.53 years	CES-D scale	MedDiet score	**Model 1**: adjusted for age, sex, education, total caloric intake, and use of depressant medications **Model 2**: adjusted for Model 1 + cardiovascular conditions*	Not associated (based on model 1; p=0.71)

y.o = years old; GDS = Geriatric Depression Scale; MCI = Mild Cognitive Impairment; MDS = Mediterranean Diet Score; BMI = Body Mass Index; T2DM = type 2 diabetes mellitus; CHD = Coronary Heart Disease; *hypertension, diabetes, myocardial infarction and stroke

Table 2. JBI Critical Appraisal Checklist for Cohort Studies

No.	JBI Critical Appraisal Checklist for Cohort Studies	Mamalaki et al. (2022)	Bardinet et al. (2022)	Cherian et al. (2020)
1.	Were the two groups similar and recruited from the same population?	N/A*	N/A*	N/A*
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	N/A*	N/A*	N/A*
3.	Was the exposure measured in a valid and reliable way?	Y	Y	Y
4.	Were confounding factors identified?	Y	Y	Y
5.	Were strategies to deal with confounding factors stated?	Y	Y	Y
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Y	Y	Y
7.	Were the outcomes measured in a valid and reliable way?	Y	Y	Y
8.	Was the follow-up time reported and sufficient to be long enough for outcomes to occur?	Y	Y	Y
9.	Was the follow-up complete, and if not, were the reasons for loss to follow-up described and explored?	Y	Y	Y
10.	Were strategies to address incomplete follow-up utilized?	N/A	Y	N/A
11.	Was appropriate statistical analysis used?	Y	Y	Y

Y = yes; N = no; N/A = not applicable, UN = unknown; *The study does not categorize participants into groups

DISCUSSION

Among the three articles retrieved from the PubMed, ProQuest, ScienceDirect, and Google Scholar databases that met the inclusion criteria for this review, only one reported a correlation between adherence to the MeDi and depressive symptoms, while the remaining two did not find such a relationship.

Mamalaki et al. analyzed the relationship between adherence to the MeDi and depression incidence among older individuals living in central Greece over at least 3 years. This study assessed MeDi using the MedDietScore based on the consumption of 11 food groups, with a higher score indicating greater adherence. Depression symptoms were assessed using the Geriatric Depression Scale (GDS), with a score of ≥6 on the GDS and/or the use of antidepressants. The same criteria were applied to exclude individuals with depression at baseline. With the average MedDietScore of 33.7±4.5 points, 23,98% of participants experienced depression at follow-up. The findings revealed that greater MeDi adherence was associated with a 6.2% reduction in the risk of depression ($p<0.001$). When comparing the highest and lowest tertiles of MeDi, each unit increase of MedDietScore

corresponded to a 46% decrease in depression risk. Additionally, the study showed that consumption of specific food groups decreases the risk of depression. Every portion increase in fruit and alcoholic beverages led to a 15.2% and 31.3% decrease in depression risk, respectively ($p < 0.05$ for both). This study also analyzes other models to account for cognitive status (dementia and MCI), finding no association between dementia and MCI diagnoses to the relationship between MeDi adherence and the risk of depression.[12]

Bardinet et al. investigated the relationship between adherence to the MeDi and the occurrence of depressive symptoms over 15 years period among older adults in France. MeDi-Lite scoring was used to assess the MeDi adherence and divided into tertiles to define three levels of adherence. Depressive symptoms were evaluated using the CES-D scale by a neuropsychologist, with a score ≥16 at least once over time and/or the use of antidepressant treatment. The results indicated that higher MeDi adherence did not show a significant association with reduced odds of depressive symptoms over time ($p=0.404$). However, when focusing on participants with a CES-D score ≥16 regardless of medication usage, the association was borderline significant ($p=0.053$). The inclusion of antidepressant treatment may introduce bias as they are also prescribed for other reasons, despite the findings being marginally significant. The researchers also performed additional analysis by using sex-specific French cutoffs (≥17 for men and ≥23 for women), which similarly did not yield significant outcomes. Furthermore, they utilized two additional scoring methods to evaluate MeDi adherence, the MDS and the MedDietScore, both of which produced consistent findings, supporting the study's conclusion and minimizing bias.[13]

The study by Cherian et al. showed no association between adherence to the MeDi and depressive symptoms, measured by a 10-item version of the CES-D scale over time ($p = 0.71$) when compared to 3 other dietary patterns (DASH diet, MIND diet, and Western diet). In contrast, individuals with the highest DASH diet scores were significantly less likely to screen positive for depressive symptoms. Both the MeDi and DASH diets encourage the intake of vegetables, fruits, legumes, whole grains, and nuts.[14] However, the MeDi includes healthy fats from sources such as olive oil and fatty fish, without specific sodium restrictions, whereas the DASH diet emphasizes reducing total and saturated fats, as well as sodium intake.[15] The dietary questionnaires used in this study included only limited questions concerning specific dietary components and their consumption frequency. For

instance, each of the following items – nuts, berries, beans, and olive oil – was addressed by a single question. This lack of additional details could lead to misunderstandings and make comparisons between them difficult.[14]

Conducting research on the elderly population may be challenging. Elderly individuals suffering from depression often exhibit some degree of cognitive decline, and conversely, those with dementia or MCI commonly experience mood disorders. Moreover, with increasing age and age-related health issues, subtle mood changes may occur, which are often overlooked as typical signs of aging. Depressive symptoms may also present atypically, such as loss of appetite, insomnia, lack of energy, cognitive deficits, psychomotor retardation, gastrointestinal complaints, and aggressive behavior, potentially leading to misclassification bias.[16] Furthermore, there can be a greater likelihood of recall errors when using self-assessments for depressive symptoms and frequency of food consumption among older adults.[17] The study by Mamalaki et al. addresses this by adjusting their variable model for patients with dementia and MCI.[12] Some studies attempted to reduce this bias by including professionals during the interview process, such as nutritionists and psychologists.[12,13]

The selection of measurement tools is crucial in structuring studies, as each tool must be adjusted to the population and validated. The tools used to assess depression and adherence to the MeDi were originally developed in English. Mamalaki et al. utilized a specific version of the GDS in their country's language while other studies did not provide details about the languages used.[12] This raises concerns about the MeDi adherence measurements, which might be less compatible in non-Mediterranean countries, such as the USA. An example of a specific tool for the US population is the Mediterranean Eating Pattern for Americans III (MEPA-III).[18]

Furthermore, the use of different scoring systems for MeDi adherence across studies, such as the MedDiet score, MDS, and MeDi-Lite, may create a difference in the evaluation. This is due to differences in the food components included in the scoring, even in the frequency and portion sizes/servings of each food component consumed. A more comprehensive scoring that includes 11-item food components with each portion size specified in grams, may be necessary for a more accurate analysis of the association.

Other than the MeDi scoring difference, the depression scoring method also differed from one to another, potentially leading to varying results. Mamalaki et al. utilized the GDS, a

depression screening tool designed only for older adults.[12,19] The GDS has several versions, and the one used in this study has been previously validated in the Greek population. In this study, the short form consisting of 15 questions was used, where a score of 6/7 was determined to be the best cut-off score for diagnosing depression in an elderly Greek population, demonstrating a specificity of 95.24% and a sensitivity of 92.23%. In the other two studies, the CES-D scale was used, either the 20-item or 10-item version, to screen for depression in general population epidemiological studies and primary care settings.[13,14] The predictive validity of all CES-D types is similar to that of the GDS, although the longer version is generally preferred over the shorter one in practice. When compared to the GDS, the CES-D scale exhibits lower sensitivity (82%) and specificity (78%).[19]

CONCLUSION

The review conducted does not provide definitive evidence that long-term adherence to the Mediterranean diet reduces the risk of depression in the elderly. The studies analyzed were cohort studies that utilized different research procedures, assessments of depressive symptoms, and measurements of adherence to the Mediterranean diet. Most results indicated no significant association between the Mediterranean diet and depression over time. However, due to the conflicting results, limited studies, and specific measurement tools suited to the age and country of the populations studied, additional research is necessary to clarify the relationship between depressive symptoms and adherence to the Mediterranean diet in this patient group.

REFERENCES

1. WHO. Depressive disorder (depression), https://www.who.int/news-room/fact-sheets/detail/depression (2023, accessed 6 November 2024).
2. Zhao Y, Wu X, Tang M, et al. Late-life depression: Epidemiology, phenotype, pathogenesis and treatment before and during the COVID-19 pandemic. *Front Psychiatry*; 14. Epub ahead of print 2023. DOI: 10.3389/FPSYT.2023.1017203.
3. Husain-Krautter S, Ellison JM. Late Life Depression: The Essentials and the Essential Distinctions. *Focus (Am Psychiatr Publ)* 2021; 19: 282–293.
4. Marx W, Moseley G, Berk M, et al. Nutritional psychiatry: the present state of the evidence. *Proc Nutr Soc* 2017; 76: 427–436.
5. Marx W, Lane M, Hockey M, et al. Diet and depression: exploring the

biological mechanisms of action. *Mol Psychiatry* 2021; 26: 134–150.

6. Liao Y, Xie B, Zhang H, et al. Efficacy of omega-3 PUFAs in depression: A meta-analysis. *Transl Psychiatry*; 9. Epub ahead of print 1 December 2019. DOI: 10.1038/S41398-019-0515-5.
7. Swainson J, Reeson M, Malik U, et al. Diet and depression: A systematic review of whole dietary interventions as treatment in patients with depression. *J Affect Disord* 2023; 327: 270–278.
8. Mrozek W, Socha J, Sidorowicz K, et al. Pathogenesis and treatment of depression; role of diet in prevention and therapy. Review. *Nutrition* 2023; 115: 112143.
9. Rudzińska A, Perera I, Gryglewska B, et al. Can the Mediterranean diet decrease the risk of depression in older persons - a systematic review. *Psychiatr Pol* 2023; 57: 339–354.
10. Martin J. Joanna Briggs Institute 2017 Critical Appraisal Checklist for Cohort Studies.
11. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *The BMJ*; 372. Epub ahead of print 29 March 2021. DOI: 10.1136/BMJ.N71.
12. Mamalaki E, Ntanasi E, Hatzimanolis A, et al. The Association of Adherence to the Mediterranean Diet with Depression in Older Adults Longitudinally Taking into Account Cognitive Status: Results from the HELIAD Study. *Nutrients* 2023; 15: 359.
13. Bardinet J, Chuy V, Carriere I, et al. Mediterranean Diet Adherence and Risk of Depressive Symptomatology in a French Population-Based Cohort of Older Adults. *Nutrients*; 14. Epub ahead of print 1 October 2022. DOI: 10.3390/NU14194121.
14. Cherian L, Wang Y, Holland T, et al. DASH and Mediterranean-Dash Intervention for Neurodegenerative Delay (MIND) Diets Are Associated With Fewer Depressive Symptoms Over Time. *J Gerontol A Biol Sci Med Sci* 2021; 76: 151–156.
15. Panbehkar-Jouybari M, Mollahosseini M, Salehi-Abargouei A, et al. The Mediterranean diet and dietary approach to stop hypertension (DASH)-style diet are differently associated with lipid profile in a large sample of Iranian adults: a cross-sectional study of Shahedieh cohort. *BMC Endocr Disord*; 21. Epub ahead of print 1 December 2021. DOI: 10.1186/S12902-021-00856-W.

16. Devita M, De Salvo R, Ravelli A, et al. Recognizing Depression in the Elderly: Practical Guidance and Challenges for Clinical Management. *Neuropsychiatr Dis Treat* 2022; 18: 2867–2880.
17. Rhodes S, Greene NR, Naveh-Benjamin M. Age-related differences in recall and recognition: a meta-analysis. *Psychon Bull Rev* 2019; 26: 1529–1547.
18. Hutchins-Wiese HL, Bales CW, Porter Starr KN. Mediterranean diet scoring systems: understanding the evolution and applications for Mediterranean and non-Mediterranean countries. *Br J Nutr* 2022; 128: 1371–1392.
19. Park SH, Lee H. Is the center for epidemiologic studies depression scale as useful as the geriatric depression scale in screening for late-life depression? A systematic review. *J Affect Disord* 2021; 292: 454–463.