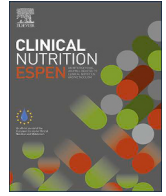




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Meta-analysis

# Effect of extra virgin olive oil on mild cognitive impairment and dementia in older adults: a systematic review and meta-analysis of clinical trials

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## SUMMARY

**Background:** Extra virgin olive oil (EVOO) has been investigated as a potential dietary strategy for cognitive health due to its neuroprotective properties. This systematic review and meta-analysis evaluated the potential impact of EVOO as an adjunct intervention for older adults within the spectrum of mild cognitive impairment (MCI) and dementia.

**Methods:** A comprehensive search was conducted across nine databases for randomized controlled trials (RCTs) that compared EVOO to a control group in older adults with MCI and/or dementia. Statistical analysis used random-effects models to determine mean differences (MD) and standardized mean differences (SMD), with the risk of bias assessed using Cochrane Risk of Bias (RoB2) and quality of evidence assessed using the GRADE tool.

**Results:** Five studies met the inclusion criteria ( $n = 747$  participants). Meta-analysis showed a significant, albeit preliminary, improvement in global cognitive function scores with EVOO consumption, including the Mini-Mental State Examination (MD = 0.42, 95 % CI = 0.15–0.68;  $p = 0.002$ ), Clock Drawing Test (MD = 0.47, 95 % CI = 0.15–0.78;  $p = 0.004$ ), and the Alzheimer's Disease Assessment Scale-Cognitive Subscale (MD = 1.45, 95 % CI = 0.39–2.51;  $p = 0.007$ ). The overall pooled effect was SMD = 0.29 (95 % CI = 0.18–0.41;  $p < 0.0001$ ). However, the certainty of evidence was rated as low according to GRADE, and the small number of trials limits the robustness of these findings.

**Conclusion:** The findings suggest a potential association between EVOO consumption and improvement in global cognitive function among older adults within MCI and dementia. Due to the low certainty of evidence, small sample sizes, and the lack of established clinical significance, these results should be interpreted with caution, and further larger-scale RCTs are required.

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## 1. Introduction

Population aging represents one of the most significant global demographic shifts of the 21st century, a phenomenon intrinsically linked to the exponential rise in the prevalence of chronic

non-communicable diseases, particularly dementia [1]. Dementia, including its prodromal stage of mild cognitive impairment (MCI), imposes a substantial burden on individuals and society by significantly elevating the risks of morbidity and mortality while progressively eroding patient autonomy [2,3]. MCI represents the clinical transitional state between the expected cognitive changes of normal aging and the early manifestations of dementia [4]. Hence, cognitive decline is further defined as the longitudinal and progressive deterioration of these cognitive abilities compared to an individual's previous level of functioning. Furthermore,

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dementia denotes a clinical syndrome characterized by significant cognitive impairment in one or more domains that is severe enough to interfere with independence in everyday activities [5]. Consequently, the associated social, familial, and financial costs of managing and caring for these patients are immense and escalating [6]. Given the clear limitations of current pharmacological treatments, which at best offer modest and transient symptomatic relief, the investigation of alternative preventive and therapeutic strategies has become a public health priority to improve and/or preserve global cognitive functioning [7,8].

Global cognitive functioning involves the integrated performance across multiple cognitive domains – including memory, orientation, language and executive functions – that translate into the ability to perceive and react, process and understand, make decisions and produce appropriate responses to the environment [9], typically assessed through validated psychometric instruments [10,11].

In this context, attention has shifted towards the potential of nutraceuticals, bioactive compounds, and functional foods in modulating brain health [12,13]. Among these, extra virgin olive oil (EVOO), a cornerstone of the Mediterranean diet, has emerged as a promising candidate, garnering considerable scientific interest for its potential neuroprotective properties [14]. Relationship between phenolic compounds and neuroprotection shows positive results in both *in vivo* and *in vitro* studies. EVOO appears to reduce the aggregation of amyloid- $\beta$  plaques, with positive cognitive effects. A randomized clinical trial demonstrated that EVOO can reduce the inflammation profile in adults, a phenomenon that also influences the genesis of MCI and Alzheimer's Disease (AD) [15]. In 2013, another randomized controlled trial concluded that EVOO intake resulted in an improvement in cognitive function, compared to the control group at a 78-month follow-up [16]. In addition, studies *in vivo* also indicate neuroprotective and therapeutic factors of EVOO [17].

Nevertheless, there is no meta-analysis on the topic performing a comprehensive analysis with randomized clinical trials, thus it is unclear whether EVOO affects outcomes in MCI/dementia. In this sense, some authors demanded further studies with more rigorous methods to investigate these findings and guide clinical applications [14–16,18–25]. Therefore, the scarcity of specific research in older adults and the relevance of this non-pharmacological intervention reinforces the importance of this study to expose a more concrete view on the subject. Hence, this research aimed to assess the effect of EVOO on MCI and/or dementia in older adults.

## 2. Methods

This study was designed as a systematic review with meta-analysis, in accordance with the recommendations of the *Cochrane Handbook* and reported according to the *PRISMA* statement [26,27] (Table S1). The protocol was registered in PROSPERO, under registration number CRD4202459359. There were no significant deviations from the registered protocol during the execution of this research.

The research question was formulated using the acronym PICOS, as follows: What are the effects of treatment with EVOO on MCI and/or dementia in older adults? The population (P) is older adults (at least 60 years of age) with MCI and/or dementia; intervention (I) is treatment, in the form of a diet, with the ingestion of EVOO; control (C) is the absence of treatment, in the form of diet, that is, without ingestion of EVOO or other diets with minimal consumption of EVOO; the outcome (O) is the progression of MCI and/or dementia in the form of changes in the psychometric instruments and the type of study (S) are randomized clinical studies [28].

### 2.1. Search strategy and selection criteria

A search was conducted in the MEDLINE, EMBASE, SCOPUS, COCHRANE, SCIELO, LILACS, Web of Science, PsycINFO and ClinicalTrials databases. A literature search was conducted in February 2025, using terms based on the Medical Subject Heading (MeSH). The keywords “Dementia” and “Olive Oil” were combined to “Older Adults”. The search was not limited by publication date. Full search strategies are defined in Supplementary file, with additional hand-searching of reference list (Tables S2–10). Rayyan [29] was used for data management, with title, abstract and full-text screening performed by two independent reviewers (VCS and APLO). Discrepancies were resolved by discussion and, if necessary, consultation of a third and fourth reviewer (EAS).

Eligible studies were randomized controlled trials, all languages written in the Roman alphabet, that included older people with MCI and/or dementia, treated with EVOO and compared with a control group that did not receive this intervention. When studies did not specifically restrict age in the included population those in which participants had a mean age of 60 years or older were considered. In this synthesis, subjects with MCI and dementia were pooled together as they represent different stages of a pathophysiological continuum of cognitive decline, where neuroinflammation and oxidative stress – key targets of EVOO – are consistently present. In the studies, the diagnosis of dementia was considered if made according to consolidated references, such as the Diagnostic and Statistical Manual of Mental Disorders (DSM), the National Institute of Neurology and Communicative Diseases and Stroke (NINCDS) and others [30,31]. The diagnosis of MCI was considered if made by the use of screening tests, including the Montreal Cognitive Assessment (MoCA), the Mini-Mental State Examination (MMSE), the Mini-Cognitive Assessment (Mini-Cog), and the Clock Drawing Test (CDT). Additionally, eligible studies included changes in cognitive domains and global cognition assessed with validated psychometric instruments, and included well-documented progression to other forms of dementia. The intervention with EVOO were considered when clearly described. Publications were excluded if participants unable to follow instructions or they had multiple psychiatric conditions. In addition, clinical studies without proper registration of psychometric instruments were also excluded. There were no restrictions regarding the publication date of studies nor any limits based on language of publication.

### 2.2. Risk of bias assessment and quality of evidence assessment

Studies were assessed using the Cochrane Risk-of-Bias (RoB2) instrument to ensure a thorough analysis of methodological quality and bias, as recommended by the Cochrane Guide for Systematic Reviews and Meta-Analyses [32–35]. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was adopted for the assessment of the overall quality of evidence of meta-analysis [36].

### 2.3. Data synthesis

Evidence of the effects of EVOO treatment on MCI and/or dementia was summarized in tables containing the year of publication and author, the country where the study was conducted, the characteristics of the sample, the study design, the comorbidities present in the sample, the interventions used, the controls used, the number of individuals in the intervention group and the control group, the instruments used to assess outcomes related to cognitive functions, the duration of follow-up and the main

outcomes. When necessary, a density of 0.917 g/ml was used to convert grams to milliliters in the dosages of EVOO.

The RStudio© software (version 2024.04.01 + 748) was used, using the Meta (version 8.0–2) and Metasense (version 1.5–2) packages [37,38]. Data from the included studies were combined using the random-effects technique, pooled analyses were based on the DerSimonian and Laird random-effects model and the inverse variance method [39–41]. The combined effect and confidence intervals were calculated using the Wald-type method. Heterogeneity was assessed using  $I^2$  values: insignificant (<30 %), moderate (30 %–50%), substantial (50 %–90 %) and considerable (>90 %). The mean difference (MD) in the scores of the scores used to assess global cognitive function was calculated. For analyses combining different scores (e.g., MMSE, CDT, ADAS-Cog), the standardized mean difference (SMD) was calculated, as they all assess the same outcome of “global cognitive function” [10,11,42,43]. These instruments, while distinct in their scoring, share a strong correlation in detecting cognitive decline [44–49], ensuring the pooled estimate reflects a consistent biological effect on global cognitive function.

The scores generated by the difference between the baseline and post-intervention values (change values) and also the post-intervention scores were considered if the groups were not significantly different, respecting the randomization process. The combination of the change values with the post-intervention values is valid, as long as it is done under the analysis of the mean difference [50]. In the synthesis of cognitive outcomes, studies assessing MCI and dementia were pooled together in forest plots for primary analyses.

The tests used to evaluate treatment (e.g., possible changes) were analyzed following a prioritization, from first choice to last choice: MMSE, Mini-Cog, CDT, ADAS-COG, MoCA and RAVLT. Tests not included in this hierarchy were the last choice for analysis. Changes in functional aspects were also considered, if evaluated with validated instruments, such as the AD Cooperative Study-Activities of Daily Living (ADCS-ADL). The improvement in the values of the ADAS-Cog scale is represented by the decrease in the score. Thus, when the studies used this scale, the score data were multiplied by  $-1$ , to facilitate the interpretation and understanding of the findings.

We performed sensitivity analysis by excluding one study at a time to identify any studies that might disproportionately influence the results.

#### 2.4. Publication bias

Publication bias was assessed using the Doi plot instrument and the LFK index. Egger's test was considered for use if the meta-analysis included at least 10 studies, according to Cochrane guidelines.

### 3. Results

In total, 937 unique records were screened, 20 full texts assessed, and five RCTs conducted between 2014 and 2022 met the inclusion criteria for this review (Fig. 1).

A total of 747 (437 in the intervention groups and 310 in the control groups) individuals were included in this systematic review. The majority of participants were women (about 54.6 %), with a mean age between 65.5 and 74.6 years, without maximum range limitations. The studies were carried out in Italy, Greece, Spain, and the United States of America. The duration of use of the intervention (EVOO) varied, with follow-ups of 6 months [21] 1 year [14,25], 4.1 years [23] and 6.5 years [16]. All five studies reported that the use of EVOO was effective in changing scores on at

least one of the scales used. In two studies, the control group comprised individuals who received a Mediterranean diet to compare with the use of EVOO [14,25]. One study compared it to another type of olive oil [21]. In two other studies, groups using other types of intervention were included for comparison with the intervention group (extra virgin olive oil), such as Mediterranean diet supplemented with nuts and low-fat diet [16,23] (Table 1).

#### 3.1. EVOO dosage and polyphenol content

The intervention groups used extra virgin olive oil in different dosages. The maximum dosage was 1 L/week or  $\approx 143$  mL/day [16]. The minimum dosage was 21.8 mL/day, given with 5 L of EVOO every 3 months, which is part of a range of 21.8 mL–32.7 mL/day reported in one study [25]. In another study the dosage was 30 mL/day, given in 30 vials per month, each containing 30 mL of the oil [21]. The last study reported a dosage of 50 mL/day, in which participants received EVOO every 2 months along with a 50 mL dosing device [14] (Table 1).

Regarding the polyphenol content, concentrations varied from 280 mg/kg [25] to 965 mg/kg [21]. All studies [14,16,21,23,25] reported positive cognitive outcomes in at least one psychometric scale, regardless of the specific dosage or polyphenol content.

#### 3.2. Scales and psychometric instruments

The scales used to assess outcomes in the studies were quite diverse. Despite this, all studies used the MMSE [14,16,21,23,25]. Two studies used the CDT scale [14,16]. Two other studies used the ADAS-Cog scale [14,25]. Other scales were used, but without standardization.

#### 3.3. Meta-analysis

All five included studies were considered for the meta-analysis.

#### 3.4. Global cognitive function

Three studies found that EVOO was effective in improving MMSE scores [14,16,25]. One study found that EVOO was effective in improving CDT scores [16]. Two studies identified that EVOO was effective in improving ADAS-Cog scores [14,25]. One study linked the use of EVOO with improvement in the CDR scores [21]. Another study linked the use of EVOO with improvements in scores on the RAVLT and CTT scales [23] (Table 1).

As a result, the meta-analysis, including five studies [14,16,21,23,25] that assessed global cognitive function using the MMSE test, showed a statistically significant improvement in MMSE scores among older adults following EVOO use (MD = 0.42; 95 % CI = 0.15 to 0.68;  $p = 0.002$ ) (Fig. 2, A).

Other two studies [14,16] that used the CDT score, indicated a statistically significant mean difference of 0.47 points in the CDT score between older adults undergoing the EVOO intervention and control groups (95 % CI = 0.15 to 0.78;  $p = 0.004$ ), which indicates the effectiveness of EVOO in improving global cognitive function (Fig. 2, B).

Regarding the ADAS-Cog scale, two studies [14,25] demonstrated a statistically significant mean difference of 1.45 points in the ADAS-Cog score favorable to the intervention with EVOO (95 % CI = 0.39 to 2.51;  $p = 0.007$ ) (Fig. 2, C).

The meta-analysis, including all scales, showed that an overall statistically significant improvement in global cognitive function was observed among older adults following EVOO intake (SMD = 0.29, 95 % CI = 0.18 to 0.41;  $p < 0.001$ ) (Fig. 2, D).

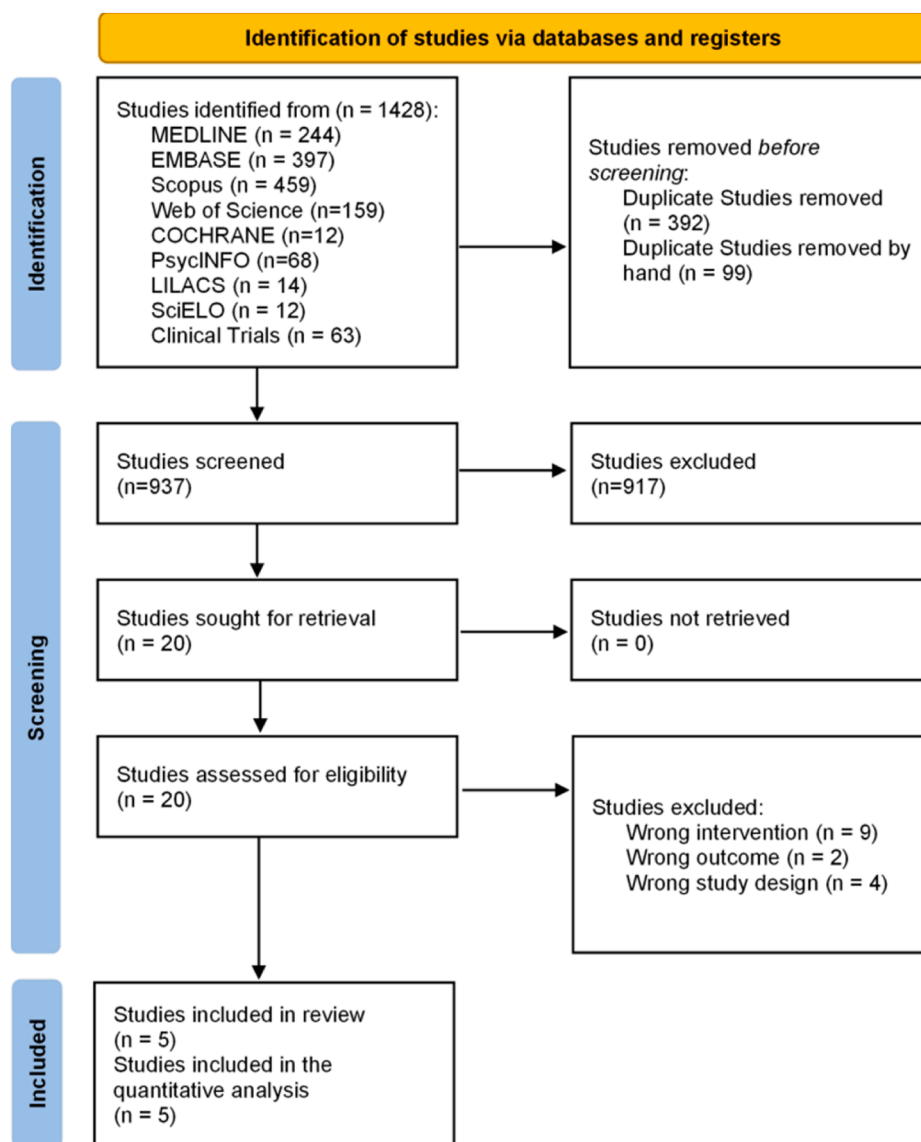


Fig. 1. Study flowchart of article selection process.

The analysis indicated low heterogeneity across all scenarios. The sensitivity analysis, by excluding each study individually, showed that statistical significance remained robust in most scenarios ( $p < 0.05$ ), except when two studies [16,23] were omitted the aggregate effect became marginally non-significant.

### 3.5. Quality of evidence

An overall low to moderate risk of bias was observed in the included studies (Fig. 3). Regarding the randomization process, only one study was classified as high risk due to the absence of reported allocation concealment procedures [25]. For deviations from intended interventions, the PREDIMED trials [16,23] were rated as having “some concerns” due to the practical impossibility of blinding participants to dietary intake in long-term interventions. All trials exhibited a low risk of bias concerning missing outcome data and the measurement of the outcome [14,16,21,23,25]. For bias in the selection of the reported result, only one study presented “some concerns” due to the lack of a publicly accessible pre-registered protocol [25].

The generated Doi plot showed low asymmetry and the LFK index reinforced the finding, with a value of  $-1.35$ . While this asymmetry is considered low and suggests a low probability of publication bias, this interpretation must be treated with caution (Fig. S1). The small number of included studies significantly reduces the statistical power of such assessments to definitively exclude the presence of publication bias. According to the GRADE, the level of evidence was low to moderate (Table S11).

## 4. Discussion

To the best of our knowledge, this systematic review and meta-analysis is the first to evaluate the effect of EVOO on mild cognitive impairment and dementia in older adults. In addition, the present study contributes to the body of available evidence by adding non-pharmacological interventions to the list of potential strategies for the treatment of the conditions addressed. This study advances the knowledge in the promising and highly pertinent disciplines of nutritional and lifestyle psychiatry. It underscores the importance of dietary interventions, particularly the incorporation or

**Table 1** Characteristics of the studies included in a systematic review and meta-analysis on the effect of extra virgin olive oil treatment on mild cognitive impairment and dementias in the older adults.

Author, year City, country	Sample characteristics	Arms	Olive Oil Group Intervention	Measurement of cognitive function outcomes	Duration of follow-up	Main Results (Intergroup)
Martínez-Lapiscina et al., 2013 Navarro, Spain	Older adults with 55–80 y of age	MedDiet + EVOO (224) MedDiet + Nuts (166)	EVOO, 1 L/week (143 mL/day)	MMSE, CDT	6.5 years	Intake of EVOO associated with better MMSE and CDT scores.
Valls-Pedret et al., 2015 Barcelona, Spain	Older adults with mean age of >65 y	MedDiet + EVOO (127) MedDiet + Nuts (112)	EVOO, 50 mL/day	MMSE, RAVLT, WMS, DGS, CTT	4.1 years	Intake of EVOO associated with better RAVLT and Color Trail test scores. NS changes in MMSE, WMS, DGS
Mazza et al., 2018 Calabria, Italy	Older adults with mean age of >65 y, MMSE >20	MedDiet + EVOO [55]	EVOO, 21.8 mL–32.7 mL/day	MMSE, ADAS-Cog	1 year	Intake of EVOO associated with better MMSE and ADAS-Cog scores
Tsolaki et al., 2020 Thessaloniki, Greece	Older adults with 60–80 y of age, MMSE >20	MP-EVOO [18] 16	HP-EVOO, 50 mL/day	MMSE, ADAS-Cog, RBMT, ROCF, TMT, DGS, LCFT, CDT	1 year	Intake of HP-EVOO associated with better MMSE, ADAS-Cog, CDT, DGS, LCFT scores. NS changes in RBMT, ROCF, TMT
Kaddoumi et al., 2022 Auburn, USA	Older adults with 55–75 y of age, MMSE 24–30	– EVOO [13]	ROO [12] EVOO, 30 mL/day	MMSE, CDR, WMS	0.5 year	Intake of EVOO associated with better CDR scores. NS changes in MMSE, WMS

Legend: RCT: Randomized Clinical Trial; EVOO: Extra Virgin Olive Oil; HP-EVOO: High Phenolic Extra Virgin Olive Oil; MedDiet: Mediterranean Diet; MMSE: Mini Mental State Examination; ADAS-Cog: Alzheimer's Disease Assessment Scale; CDR: Clinical Dementia Rating; CDT: Clock Drawing Test; RAVLT: Rey Auditory-Verbal Learning Test; WMS: Wechsler Memory Scale; RBMT: Rivermead Behavioural Memory Test - Story Immediate and Delayed Recall; ROCF: Rey Osterrieth Complex Figure test - Copy and Delayed Recall; TMT: Trail Making Test - Parts A and B; DGS: Digit Span, Wechsler Memory Scale Subtest; LCFT: Letter and Category Fluency Test; CTT: Color Trail Test - Parts 1 and 2. The conversion between milliliters to grams in Olive Oil dosage was made considering the density of 0.917 g/mL.

increased intake of specific foods like extra-virgin olive oil (EVOO), to enhance neurophysiological mechanisms underlying global cognitive function. These results also bear considerable relevance for geriatric and clinical psychiatric practice. Our findings suggest that the consumption of EVOO was associated with statistically significant improvements in global cognitive function scores in older adults.

Our pooled analysis indicates a positive effect of EVOO intake and improvements in global cognitive function in adults with 60 years old or more. This confirms the direction of effect suggested by a prior systematic review [19], which identified a positive outcome but was unable to substantiate it quantitatively due to considerable heterogeneity and methodological inconsistencies among the available studies [19]. However, the present study successfully addressed these specific limitations, which reduced heterogeneity and permitted the quantitative synthesis of data, revealing a statistically significant benefit for global cognitive function. As such, our study represents the first meta-analysis of randomized controlled trials in this field to provide a preliminary evidence that may inform future clinical practice.

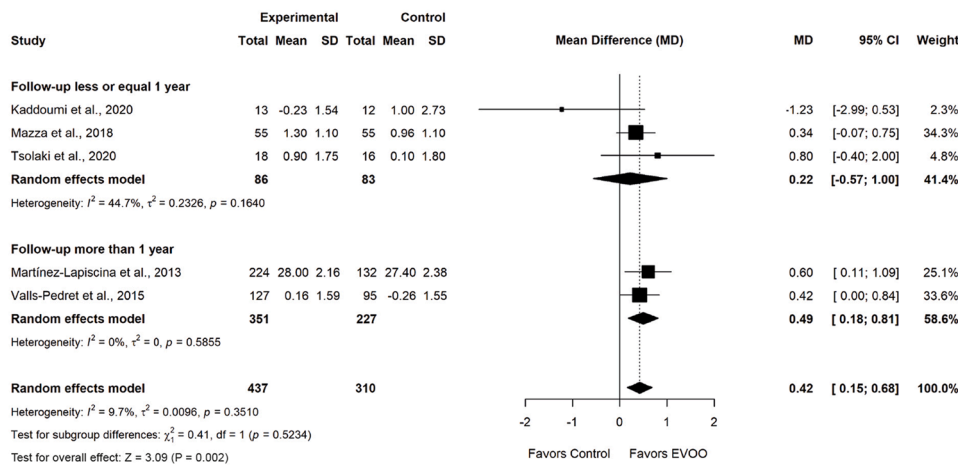
It is essential to distinguish between statistical significance and clinical relevance. Although our meta-analysis demonstrated statistically significant improvements in cognitive scores, these results must be evaluated against the Minimum Clinically Important Difference (MCID). For the MMSE, an improvement of 2–4 points is generally considered clinically meaningful in dementia populations [51,52]. Our observed mean difference of 0.42 does not reach this threshold. Similarly, for the ADAS-Cog, where MCID is 2–3 points for MCI patients and 3 points for AD patients, our findings showed a mean difference of 1.45 points [53].

Our findings regarding EVOO appear promising, especially within a landscape where other nutritional interventions have shown mixed results. For instance, omega-3 fatty acid supplementation, despite having a strong biological rationale, has failed to yield a significant effect on cognition [54]. Similarly, a meta-analysis with 702 individuals investigating the association between omega-3 fatty acids and global cognitive function with ADAS-Cog in older adults with Alzheimer's Disease (AD) found no significant benefits from supplementation [55]. Recent meta-analyses have reported conflicting conclusions regarding the effects of curcumin in the management of MCI and/or dementia [56–59]. However, direct comparisons between EVOO and these compounds cannot be made based on the present data. A significant practical advantage of EVOO is its nature as a food; introducing or increasing the consumption of a culinary oil used worldwide is far more feasible than adding another supplement capsule to an older adult's daily regimen. Given the prevalence of polypharmacy in this demographic, increasing the pill burden can significantly reduce treatment adherence, making a dietary intervention like EVOO a more sustainable and patient-friendly strategy.

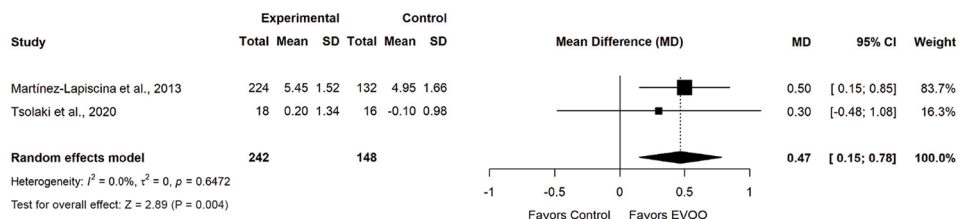
Other nutraceuticals evaluated for the treatment or prevention of MCI include antioxidant vitamins and metabolic cofactors, notably vitamin E and acetyl-L-carnitine (ALCAR). However, a Cochrane review found no evidence that vitamin E reduces the risk of progression from MCI to dementia or improves global cognitive function in patients with established AD [60]. The success of EVOO may be related to its pleiotropic nature, whereby its polyphenols act simultaneously to suppress inflammation, reduce metabolic stress, and potentially interfere with amyloid pathways [61].

From the five RCTs, only two studies used more precise methods for measuring and standardizing the amount of EVOO ingested [14,21]. Both studies showed that EVOO was effective in improving global cognitive function. Consequently, establishing a

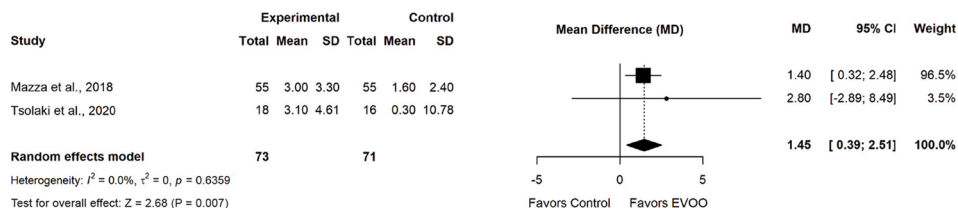
## A | Mini-mental State Examination



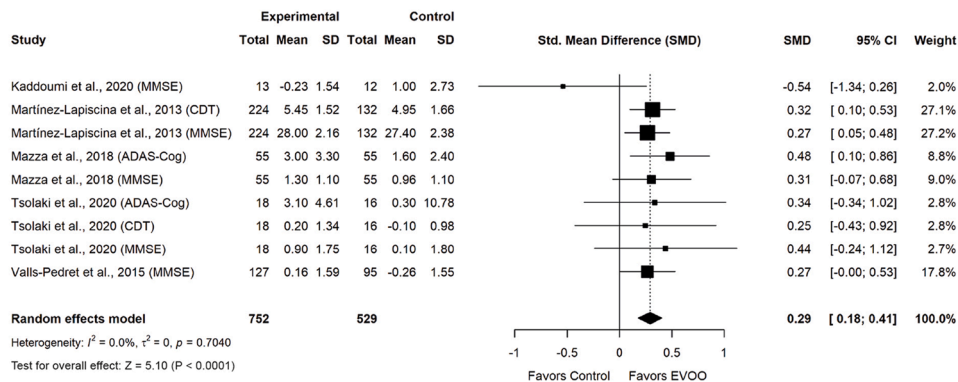
## B | Clock Draw Test



## C | Alzheimer's Disease Assessment Scale



## D | Combined Scales



clear dose–response relationship proved challenging, owing to the considerable heterogeneity in both the dosage and duration of the interventions. Our findings indicate a wide therapeutic window, with doses as low as 22 mL/day containing 280 mg/kg of polyphenols [25], as well as higher doses of 143 mL/day [16]. However, the included trials did not use a uniform method for reporting polyphenol fractions. Therefore, it is currently not possible to determine the optimal therapeutic dosage of EVOO for cognitive neuroprotection based on the available evidence.

The follow-up durations in the included trial ranged from 6 months [21] to 6.5 years [16]. A narrative synthesis suggest that while short-term effects are detectable, longer follow-up periods yielded more reliable data regarding the intervention's effects [16,23]. Given that neurodegenerative processes are protracted phenomena that unfold over decades, it is biologically plausible that nutritional interventions necessitate extended follow-up periods to elicit cognitive changes of a magnitude detectable by psychometric assessments.

The neuroprotective effects of EVOO are largely attributed to its rich profile of bioactive polyphenolic compounds [24]. Prominent examples include oleocanthal, known for its potent anti-inflammatory activity, and hydroxytyrosol, a powerful naturally occurring antioxidant [15,22]. These compounds are hypothesized to exert therapeutic effects by directly counteracting key pathophysiological mechanisms central to neurodegeneration, namely by mitigating neuroinflammation and combating oxidative stress [24]. Specifically, they may mitigate neuroinflammation, combat oxidative stress, and attenuate amyloid- $\beta$  (A $\beta$ ) aggregation and pathologies. These processes—neuroinflammation, oxidative stress, and A $\beta$  aggregation—are all well-established hallmarks implicated in the onset and progression of MCI and AD. Also, EVOO can directly improve synaptic activity, short-term plasticity, and memory while decreasing tau neuropathology [62]. This modulation represents a plausible biological mechanism for the cognitive improvements observed in this review.

Furthermore, the neuroprotective potential of EVOO is grounded in pleiotropic biological mechanisms that stabilize cardiovascular function, enhance blood–brain barrier (BBB) integrity, and modulate inflammatory signaling [15,63–67]. EVOO provides indirect neuroprotection by ensuring consistent cerebral blood flow and reducing vascular risks such as atrial fibrillation, which decreases the incidence of silent cerebral infarcts—a primary driver of cognitive decline [63,65]. Moreover, daily EVOO consumption has been shown to reduce BBB permeability, facilitating the clearance of metabolic waste and neurotoxins [21]. These vascular effects are complemented by the modulation of the platelet-activating factor (PAF) pathway, where polar lipids in the oil act as natural antagonists to the PAF receptor (PAF-R), suppressing pro-inflammatory cascades (such as NF- $\kappa$ B) and inhibiting the release of neurotoxic cytokines (IL-1 $\alpha$  and TNF- $\alpha$ ) [64–67].

This review has some limitations. The primary limitation was the substantial diversity of psychometric instruments employed in the included studies for assessing both global cognitive function and specific cognitive domains, as shown in Table 1. While all studies utilized the Mini-Mental State Examination (MMSE), the majority employed a battery of more than three instruments for their assessments [14,16,21,23]. Although these instruments are all capable of detecting changes in cognitive function, the methodological diversity and lack of standardization in the tests applied

compromise the quality of the results and the overall strength of the evidence. The standardized application of psychometric assessment tools is crucial for advancing knowledge in this field.

Although an exhaustive search was conducted, only three of the included studies focused exclusively on MCI populations [14,21,25], while the remaining trials evaluated age-related cognitive decline in broader cohorts, without providing independent, extractable data for a pure dementia subgroup [16,23]. Consequently, these populations were analyzed together as a continuum of cognitive impairment. While this approach is biologically supported by the shared neurodegenerative hallmarks targeted by EVOO polyphenols, we acknowledge that the lack of diagnosis-specific data limits our ability to determine if the magnitude of the effect differs significantly between MCI and established dementia.

Due to the unestablished methodology for the analysis of EVOO treatment and for the design of RCT evaluating outcomes related to MCI and dementia in the elderly, the variability in the interventions across the included studies constitutes a limitation. EVOO doses varied considerably (from 21.8 to 143 mL/day). The control groups were heterogeneous, making it difficult to isolate the specific effect of EVOO. In addition, a moderate overall risk of bias was found across the studies.

Regarding the meta-analysis process, the small number of studies included ( $n = 5$ ) should also be considered a limitation that restricts the statistical power and the robustness of the pooled estimates. This constraint limits our ability to generalize the findings and necessitates that the observed effect sizes (i.e. SMD = 0.29) be interpreted with substantial caution. Also, it is crucial to note that the overall certainty of evidence was rated as low, according to the GRADE approach. This low certainty stems from the small number of included trials, the moderate to high risk of bias, and the limited total numbers of participants. The presence of a high risk of bias [25] in RoB2 introduces a potential for overestimation of the true therapeutic effect. Given the small number of included studies, the overall SMD is highly sensitive to the internal validity of each trial. Also, the small number of trials restricts our ability to conduct a robust assessment of publication bias, although the LFK index suggested only low asymmetry. Therefore, while EVOO remains promising dietary adjunct, current findings should be viewed as preliminary rather than definitive evidence of clinical efficacy, as the true effect size could be substantially different if only low-risk, large-scale trials were available for synthesis. This alignment with the GRADE “low certainty” rating underscores the preliminary nature of current clinical recommendations.

Future research should employ more robust methodologies, incorporating: [1] the standardized use of validated scales, such as the MMSE and the ADAS-Cog, for assessing global cognitive function; [2] extended follow-up periods of at least 24 months; and [3] detailed characterization of the EVOO intervention – as was commendably performed by all articles included in this review – with a comprehensive description of its polyphenol profile, fatty acid composition, and acidity. Furthermore, longitudinal studies that include detailed assessments of overall dietary patterns are needed to provide stronger evidence for long-term associations.

In terms of practical recommendations, incorporating EVOO into the daily diet can be encouraged through simple methods. Although the included trials showed heterogeneity in dosages

**Fig. 2.** Forest plot of the effects of Extra Virgin Olive Oil (EVOO) on global cognitive function and specific psychometric scales.

Legend: (A) Mini-Mental State Examination (MMSE) analysis stratified by follow-up duration ( $\leq 1$  year vs.  $> 1$  year). (B) Clock Drawing Test (CDT) analysis. (C) Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog) analysis. (D) Combined analysis of all scales assessing global cognitive function (Standardized Mean Difference – SMD). Note: Data for the ADAS-Cog score (Panel C) were multiplied by  $-1$  so that positive values indicate improvement favoring the EVOO intervention, ensuring consistency with the other scales.

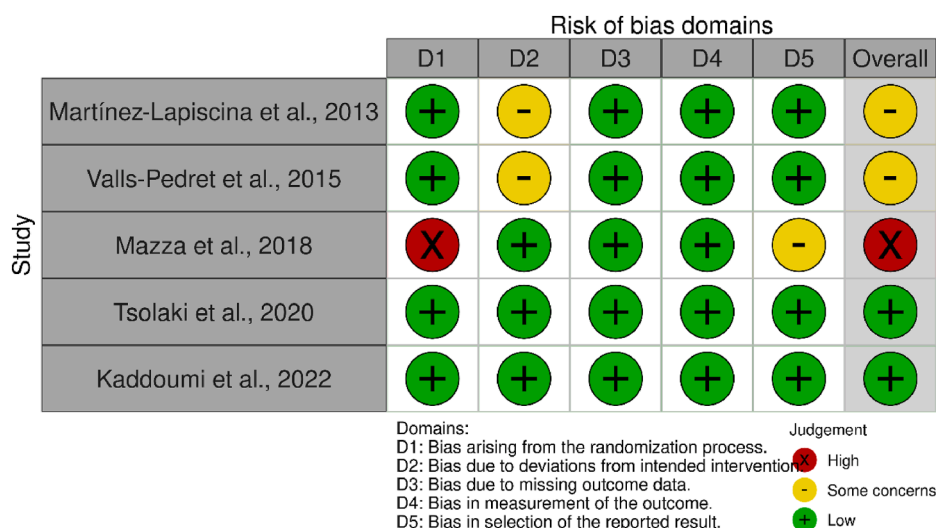


Fig. 3. Risk of bias summary for the included randomized controlled trial.

(from 21.8 mL/day to 143 mL/day), the minimum dose associated with benefits was approximately 22 mL/day (about two table-spoons) [25]. Practical ways to increase consumption include its use at breakfast as a substitute for butter or margarine, and as the primary dressing for salads and vegetables, either raw or added after cooking. To maximize benefits, EVOO's profile of bioactive compounds, such as polyphenols, should be preserved. Therefore, consumption at room temperature (cold) is preferentially recommended, avoiding heating at high temperatures, which can degrade these key compounds. Finally, it is essential to align expectations regarding the temporality of the effects. Unlike pharmacological interventions, nutritional strategies require time; study follow-ups ranged from six months to 6.5 years [16,21]. This indicates that EVOO's efficacy likely depends on continuous and prolonged use for detectable cognitive changes to occur, as suggested by the long-term nature of nutritional interventions.

## 5. Conclusion

The use of EVOO was associated with a statistically significant improvement in global cognitive function scores in older adults. These findings suggest that EVOO may represent a potential nutraceutical strategy for MCI and dementia management, although further robust clinical trials are needed to confirm efficacy and establish standardized dosages.

## Registration and protocol

The protocol of this work can be fully assessed in the PROSPERO platform by the register code **CRD4202459359**.

## Data availability statement

The authors confirm that all data supporting the findings of this study are available within the main text and/or supplementary material.

## Declaration of sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Declaration of conflicts of interest

All authors declare that they have no conflicts of interest.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnesp.2026.102977>.

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