

Olive Oil and Longevity: A Review of Evidence Linking Mediterranean Fats to Healthy Aging

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Abstract

Background: Olive oil, particularly extra virgin olive oil (EVOO), is a key component of the Mediterranean diet and has been associated with reduced mortality and lower incidence of age-related diseases. Its rich content of monounsaturated fatty acids (MUFA) and polyphenolic compounds such as hydroxytyrosol and oleuropein suggests a multifactorial role in promoting healthy aging and longevity.

Methods: A narrative review was conducted by synthesizing data from mechanistic studies, epidemiological cohorts, randomized controlled trials (RCTs), and meta-analyses published over the past two decades. Databases including PubMed, Scopus, and Web of Science were searched for studies examining the effects of olive oil on aging biomarkers, chronic disease risk, and mortality.

Results: Olive oil demonstrates antioxidant, anti-inflammatory, cardioprotective, and neuroprotective properties through several biological pathways. These include modulation of oxidative stress via Nrf2 activation, suppression of pro-inflammatory signaling such as NF-κB, improvement of endothelial function, and regulation of longevity-associated genes (e.g., sirtuins and FOXO). Epidemiological evidence from the PREDIMED trial and large-scale cohorts such as EPIC and the Nurses' Health Study reveals inverse associations between olive oil consumption and all-cause mortality, cardiovascular disease, neurodegeneration, and certain cancers. Additionally, olive oil appears to positively influence key hallmarks of aging, including mitochondrial dysfunction, inflammaging, and cellular senescence.

Conclusions: The current body of evidence supports olive oil as a functional dietary fat with potential to enhance healthspan and longevity. While observational and short-term interventional studies are promising, further long-term RCTs and systems biology approaches are needed to refine intake recommendations and explore inter-individual responses. Incorporating high-quality olive oil into dietary patterns may serve as an accessible strategy to promote healthy aging and reduce the burden of chronic disease.

Keywords: Olive oil; extra virgin olive oil; Mediterranean diet; longevity; healthy aging; polyphenols; monounsaturated fatty acids; oxidative stress; inflammation; healthspan

Introduction

Olive oil remains a cornerstone of the longevity diet, especially in light of global aging populations and the rising burden of chronic diseases. Its proven cardiometabolic and anti-inflammatory benefits, central to Mediterranean dietary patterns, offer a sustainable, plant-based fat alternative aligned with both health promotion and ecological goals. As dietary trends shift toward personalized and preventative nutrition, olive oil's relevance continues to grow in both clinical and public health contexts.

The topic of longevity and healthy aging has been and continues to be a focus of the medical community and a growing one in the general community. Research spans from basic scientific mechanistic and epigenetic work to population studies. However, diet continues to shine as a modifiable and attainable goal, and, specifically, one dietary element continues to resurface for its potential benefits: olive oil. Olive oil has been a nutritional staple of many cultures for centuries, specifically cultures that seem to have better healthspan and resilience. There are so many factors in healthy aging. But what role does olive oil play? The goal of this review is to address this question head on.

Aging is without a doubt a complicated, ever-evolving state. It is a complex, multifactorial process characterized by progressive physiological decline and increased susceptibility to chronic diseases, including cardiovascular disease, cancer, neurodegenerative disorders, and type 2 diabetes. Some many argue that aging is not completely inevitable in the context of developing debilitating conditions, and, at the very least, aging is a modifiable disease-state. Lifestyle and dietary factors are now widely recognized as critical modulators of both lifespan and healthspan—the period of life spent in good health. Among dietary patterns, the Mediterranean diet has consistently been associated with reduced all-cause mortality and improved aging outcomes in epidemiological and interventional studies [1,2].

Olive oil has been a nutritional component of many cultures for centuries, specifically cultures that seem to have better healthspan and resilience. Is olive oil part of the secret of those cultures living longer and healthier lives? If so, how does it contribute and to what extent? Olive oil, particularly extra virgin olive oil (EVOO), is a hallmark of the Mediterranean diet and serves as its primary source of dietary fat. EVOO is rich in monounsaturated fatty acids (MUFA), especially oleic acid, and contains a diverse array of minor bioactive compounds including polyphenols (e.g., hydroxytyrosol, oleuropein), tocopherols, and phytosterols [3]. These components exhibit a range of biological effects, such as antioxidant activity, anti-inflammatory modulation, endothelial protection, and neuroprotection, which are increasingly linked to mechanisms of healthy aging [4–6].

Recent advances in aging biology have identified several conserved pathways and cellular hallmarks involved in the aging process, including oxidative stress, chronic low-grade inflammation ("inflammaging"), genomic instability, mitochondrial dysfunction, and altered intercellular communication [1]. Notably, the bioactive components of olive oil have been shown to target many of these mechanisms, positioning olive oil as a promising dietary intervention in the promotion of longevity.

This review aims to (1) summarize the composition and key bioactive constituents of olive oil relevant to aging, (2) explore mechanisms through which olive oil influences longevity-associated processes, and (3) evaluate clinical and epidemiological evidence linking olive oil consumption with reductions in age-related morbidity and all-cause mortality. The potential of olive oil as a functional food in aging populations is also explored, along with directions for future research.

Composition and Bioactive Compounds in Olive Oil

Extra virgin olive oil (EVOO) is more than just a healthy fat—it's a rich blend of compounds that may work together to support health and longevity (Figure1). While the majority of EVOO is made up of monounsaturated fats—mainly oleic acid—what sets it apart is its small but diverse group of minor compounds, especially phenols, which are largely removed during refining [7-9]. Among these, hydroxytyrosol, oleuropein, and oleocanthal have shown the most promise, particularly for their antioxi-

dant and anti-inflammatory effects [10,11]. Research suggests they can neutralize harmful free radicals and may influence key inflammatory pathways like COX and NF- κ B [12,13]. However, much of this evidence comes from cell or animal studies, and findings in humans remain inconsistent or preliminary. Other components, such as vitamin E and squalene, may also contribute to protective effects, though their roles are less clearly defined [14]. Overall, while some mechanisms—especially those related to antioxidant defense and inflammation—are supported by stronger data, the broader picture remains complex and evolving, calling for more rigorous human studies to confirm these potential benefits.

Figure 1: Bioactive compounds in olive oil and their effects on aging.

Compound	Class	Mechanisms of Action	Effects on Aging
Oleic acid	Monounsaturated fatty acid	Reduces LDL oxidation; improves insulin sensitivity; modulates lipid metabolism	Cardiovascular protection; metabolic regulation
Hydroxytyrosol	Polyphenol (secoiridoid)	Scavenges ROS; activates Nrf2; suppresses NF- κ B; enhances autophagy	Antioxidant defense; inflammation reduction; mitochondrial and genomic protection
Oleuropein	Polyphenol (secoiridoid)	Anti-inflammatory; modulates SIRT1 and AMPK pathways; supports DNA repair	Cellular stress resistance; improved metabolic signaling
Oleocanthal	Phenolic aldehyde	Inhibits COX-1 and COX-2; mimics NSAIDs; reduces TNF- α and IL-6	Reduces chronic inflammation ('inflammaging'); neuroprotective
Tyrosol	Simple phenol	Mild antioxidant; supports neuroprotection and endothelial function	Cognitive resilience; vascular aging protection
Squalene	Triterpene	Enhances skin barrier; antioxidant properties; protects lipids from peroxidation	Skin aging prevention; cellular membrane stability
α -Tocopherol	Vitamin E (antioxidant)	Neutralizes lipid peroxyl radicals; stabilizes membranes	Prevents lipid peroxidation and age-related oxidative damage
Phytosterols	Plant sterols	Inhibit intestinal cholesterol absorption; modulate immune responses	Cardiometabolic health; anti-inflammatory effects
Lignans	Phytoestrogens	Antioxidant; modulate estrogen receptors; reduce inflammation	Hormonal balance; reduced age-related inflammation

Mechanisms Linking Olive Oil to Longevity

Olive oil's potential to support healthy aging is thought to come from a mix of bioactive compounds that may influence key processes linked to aging and chronic disease. One of the main proposed benefits is a reduction in oxidative stress—often described as a driver of aging—through both antioxidant activity and stimulation of the body's own defense systems, like glutathione peroxidase and superoxide dismutase [15]. Some polyphenols, especially hydroxytyrosol and oleuropein, appear to activate the Nrf2 pathway, which helps cells protect themselves from damage [16]. However, much of this evidence comes from lab and animal studies, and results in human trials have been inconsistent. Similarly, olive oil's anti-inflammatory effects, particularly through the inhibition of NF- κ B and inflammatory cytokines like IL-6 and TNF- α , are promising but not yet conclusive [17]. Compounds like oleocanthal have even been likened to ibuprofen for their COX-inhibiting effects, but clinical validation

is limited [18]. Olive oil has also been linked to longevity-related pathways such as sirtuins, AMPK, and insulin signaling, though findings here are largely theoretical or based on extrapolated models [19,20]. While some studies suggest benefits for mitochondrial function and energy metabolism [21], others show minimal or no impact, especially when isolated compounds are tested rather than whole EVOO. Overall, while olive oil shows potential in targeting aging pathways, many of the mechanisms remain preliminary, and the strength of evidence varies across studies and model systems.

Epidemiological Evidence

A growing body of epidemiological research supports an association between olive oil consumption and reduced risk of chronic disease and all-cause mortality (Figure 2). One of the most cited studies, the PREDIMED (Prevención con Dieta Mediterránea) randomized controlled trial, found that individuals at high cardiovascular risk who consumed a Mediterranean diet supplemented with extra virgin olive oil (EVOO) experienced a 30% reduction in major cardiovascular events compared to a low-fat control group [2]. These findings have been echoed in several longitudinal cohort studies. For example, the EPIC (European Prospective Investigation into Cancer and Nutrition) cohort identified an inverse relationship between olive oil intake and cardiovascular and cancer-related mortality in Mediterranean populations [22]. Likewise, the Nurses' Health Study and Health Professionals Follow-Up Study in the United States reported associations between higher olive oil consumption and lower risks of mortality and chronic diseases, including neurodegenerative and cardiovascular conditions [23].

Figure 2: Epidemiologic studies demonstrating the benefits of olive on disease events and mortality

Study	Population	Key Findings	
PREDIMED (Spain)	7,447 high-risk cardiovascular adults	EVOO-enriched Mediterranean diet reduced cardiovascular events	Estruch et al., 2013
EPIC (Europe)	Over 500,000 adults across 10 European countries	Higher olive oil intake linked to lower mortality and breast cancer risk	Buckland et al., 2012
Nurses' Health Study & HPFS (USA)	Over 90,000 women and 40,000 men in the U.S.	Greater olive oil intake associated with lower all-cause and cause-specific mortality	Guasch-Ferre et al., 2022
Psaltopoulou et al. Meta-analysis	Combined multiple Mediterranean cohorts	Olive oil associated with reduced stroke, cognitive decline, and depression risk	Psaltopoulou et al., 2004

However, these observational findings should be interpreted with caution. Cohort studies are inherently limited by residual confounding from unmeasured or imprecisely measured lifestyle and dietary factors. Most rely heavily on food frequency questionnaires (FFQs), which are prone to recall bias and inaccuracies in estimating portion sizes or olive oil types. Additionally, the substitution effects seen in pooled analyses—for instance, replacing margarine or butter with olive oil—may reflect broader differences in overall dietary patterns or socioeconomic status rather than the isolated impact of olive oil itself [24]. Although a meta-analysis of over 800,000 individuals from 13 cohort studies found that higher olive oil intake was associated with reduced risks of all-cause mortality and stroke [25], the results remain observational and may not fully account for cultural, dietary, and regional variations in olive oil use, especially between Mediterranean and non-Mediterranean populations. These differences may affect the external validity of findings and limit generalizability.

Clinical Trials and Interventions

Clinical trials provide more direct evidence for olive oil's potential health benefits, particularly EVOO. The PREDIMED trial, a landmark multicenter RCT involving 7,447 participants, demonstrated cardiovascular protection and improved markers such

as lipid profiles, inflammation, and insulin sensitivity with daily consumption of 50 mL of EVOO [2,26]. Cognitive benefits were also observed in a secondary analysis, with higher EVOO intake associated with better memory and reduced risk of mild cognitive impairment [27]. Smaller RCTs have suggested improvements in endothelial function, oxidative stress, and glucose metabolism in metabolic syndrome and type 2 diabetes patients [28,29]. Mechanistic studies, such as those by Konstantinidou et al., revealed gene expression changes linked to anti-inflammatory and antioxidant pathways following EVOO consumption [30].

Nonetheless, most clinical trials to date have short follow-up periods, often lasting only weeks to months, making it difficult to assess long-term effects on aging or mortality. Sample sizes in many studies are small, and interventions vary widely in EVOO dose, duration, and baseline dietary context. Additionally, studies often take place in Mediterranean countries where olive oil is embedded in traditional food cultures, which may not reflect patterns in other regions where consumption is lower or where refined olive oil is more commonly used. These cultural and regional differences may influence both the biological response and the practical implementation of olive oil-based interventions, further complicating the translation of findings to broader populations.

In sum, while current evidence suggests that olive oil—particularly EVOO—may positively influence markers of health and longevity, methodological limitations and population differences highlight the need for longer, well-controlled trials with culturally diverse participants and aging-specific endpoints to confirm its role in promoting healthspan.

Olive Oil and Disease Prevention in Aging

The consumption of olive oil, particularly EVOO, has been consistently associated with a lower risk of age-related diseases that are major contributors to morbidity and mortality in older populations (Figure 3). These include cardiovascular disease, type 2 diabetes, neurodegenerative disorders, and cancer—conditions underpinned by chronic inflammation, oxidative stress, and metabolic dysfunction.

Cardiovascular disease (CVD) remains the leading cause of death globally, and olive oil plays a central role in cardiovascular prevention. Numerous studies, including the PREDIMED trial, have shown that a Mediterranean diet enriched with EVOO significantly reduces the incidence of myocardial infarction, stroke, and cardiovascular death [2]. Mechanisms underlying these benefits include improved lipid profiles (e.g., increased HDL-C, decreased LDL oxidation), reduced endothelial dysfunction, and inhibition of platelet aggregation [31,32].

Type 2 diabetes mellitus (T2DM) is another condition strongly influenced by dietary fats. EVOO has been shown to enhance insulin sensitivity and glucose metabolism, partly by modulating inflammatory pathways and preserving β -cell function. In the PREDIMED study, participants consuming higher amounts of olive oil had a 40% lower risk of developing T2DM over 4 years [33]. These effects are supported by smaller trials showing that olive oil-rich meals result in lower postprandial glucose and insulin levels compared to saturated-fat-rich meals [34].

Neurodegenerative diseases, particularly Alzheimer's disease (AD), are increasingly linked to oxidative stress, mitochondrial dysfunction, and neuroinflammation. Preclinical studies show that olive oil polyphenols, especially oleocanthal and hydroxytyrosol, reduce amyloid- β aggregation, enhance autophagy, and protect neuronal integrity [35]. Human trials such as the PREDIMED-NAVARRA sub-study have also reported improved cognitive function and reduced risk of cognitive decline in older adults adhering to EVOO-enriched diets [36].

Cancer prevention is another area of interest, particularly regarding breast, colorectal, and prostate cancers. Olive oil's phenolic compounds exhibit anti-proliferative, pro-apoptotic, and anti-angiogenic activities, which may contribute to reduced cancer

risk observed in epidemiological studies [37]. For example, oleuropein has been shown to inhibit tumor growth via modulation of the PI3K/Akt and MAPK pathways and by altering epigenetic gene expression patterns [38].

Together, these findings highlight olive oil as a potent dietary component for reducing the burden of chronic diseases that accompany aging. Its inclusion in the habitual diet may thus promote not only longevity but also the preservation of functional capacity and quality of life in later years.

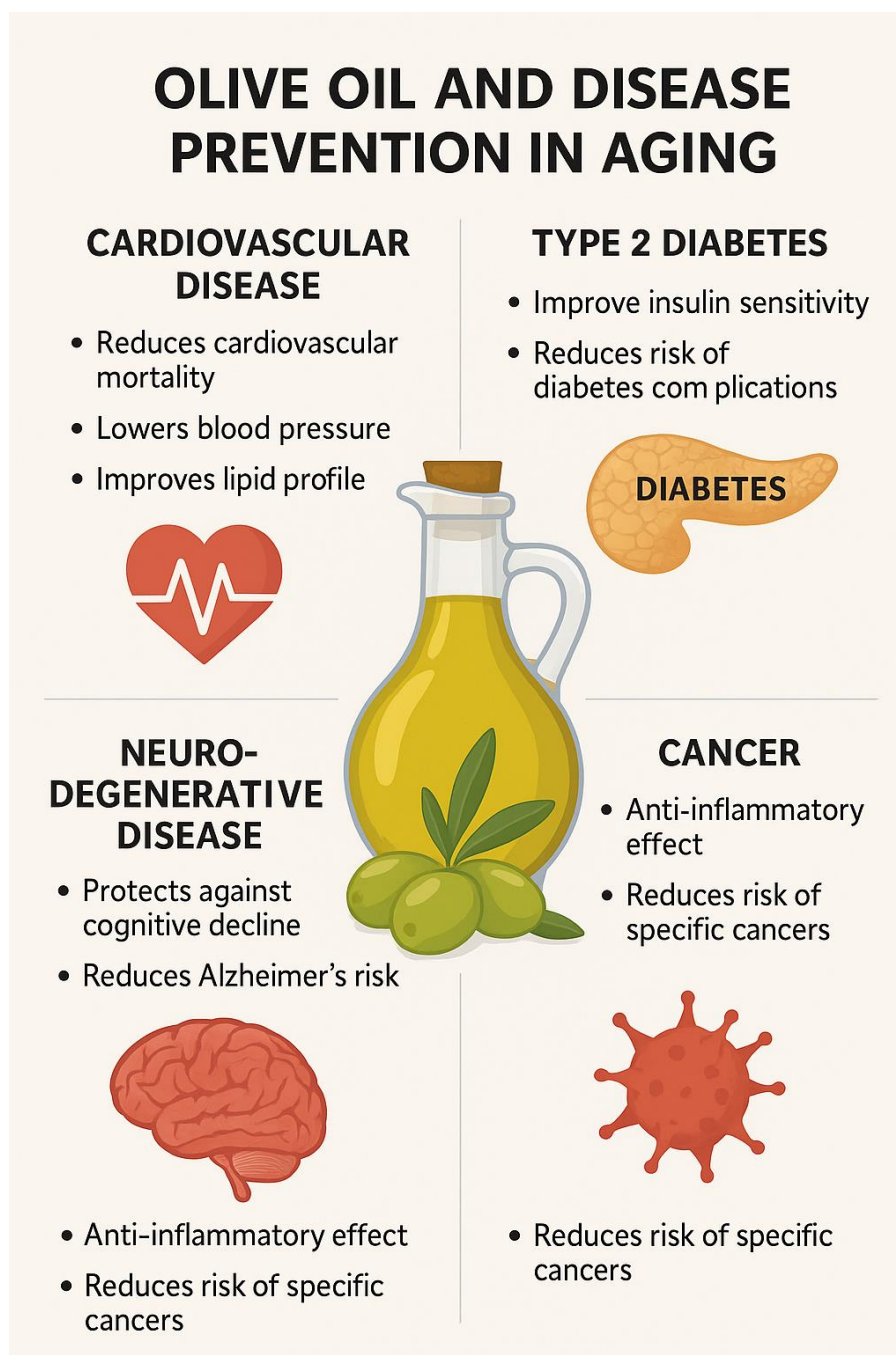


Figure 3: Olive oil and disease prevention in aging

Longevity Pathways: Olive Oil's Role in Aging Hallmarks

The aging process is increasingly understood through the lens of molecular and cellular hallmarks, including genomic instability, epigenetic alterations, mitochondrial dysfunction, cellular senescence, deregulated nutrient sensing, stem cell exhaustion,

and chronic low-grade inflammation (“inflammaging”) [1]. Bioactive compounds in olive oil, particularly those in EVOO, have been shown to influence many of these aging hallmarks through pleiotropic molecular pathways that promote healthspan and longevity (Figure 4).

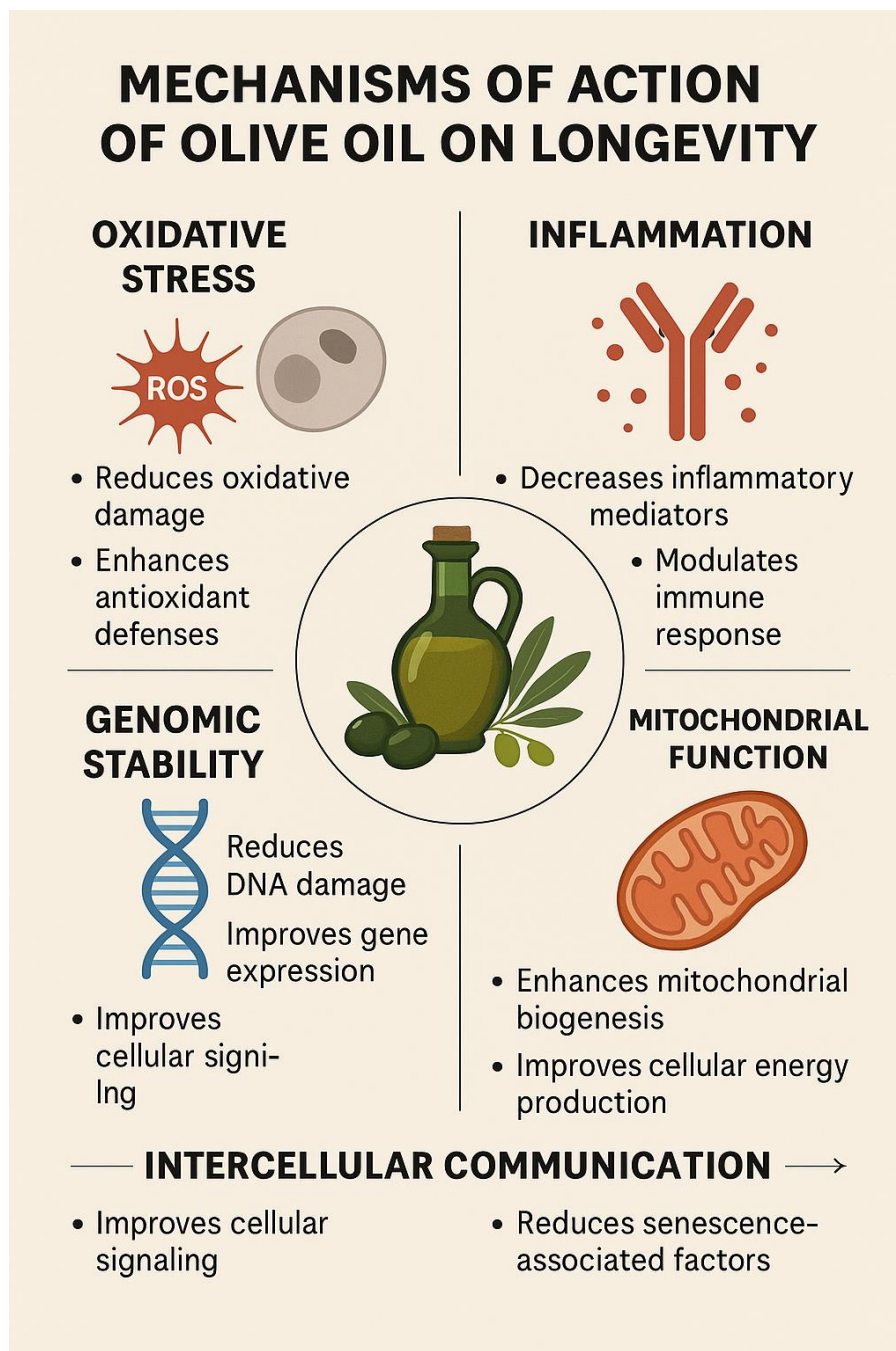


Figure 4: Potential mechanisms linking olive oil to longevity

One key target is oxidative stress, a primary contributor to genomic instability and mitochondrial damage. EVOO polyphenols such as hydroxytyrosol and oleuropein directly scavenge reactive oxygen species (ROS) and also activate the Nrf2–ARE (antioxidant response element) signaling pathway, upregulating endogenous antioxidant enzymes including glutathione peroxidase and superoxide dismutase [12,39]. These effects contribute to improved mitochondrial function and decreased DNA damage—critical mechanisms in slowing cellular aging.

Chronic inflammation, another hallmark of aging, is modulated by olive oil through suppression of pro-inflammatory media-

tors. Polyphenols and oleocanthal inhibit NF- κ B signaling and cyclooxygenase enzymes (COX-1 and COX-2), leading to decreased expression of cytokines such as IL-6, TNF- α , and IL-1 β [5,18]. This anti-inflammatory profile supports both systemic immune resilience and neuroimmune health in aging.

Olive oil also interacts with nutrient-sensing pathways such as AMP-activated protein kinase (AMPK), insulin/IGF-1 signaling, and the sirtuin family of NAD⁺-dependent deacetylases. Activation of SIRT1 by EVOO phenolics has been linked to improved metabolic efficiency, mitochondrial biogenesis, and genomic stability [40]. These pathways mirror those activated by caloric restriction—an established intervention for lifespan extension in model organisms.

Additionally, evidence suggests that EVOO modulates cellular senescence, both by reducing senescence-associated secretory phenotype (SASP) factors and by enhancing autophagy, particularly in neuronal and endothelial cells [41]. Studies have shown that hydroxytyrosol promotes autophagic clearance of damaged proteins and organelles, a process that declines with age and is critical for proteostasis [42].

Taken together, these findings position olive oil as a dietary agent capable of influencing multiple aging-related pathways. By modulating oxidative stress, inflammation, nutrient sensing, and cellular quality control, olive oil may not only reduce disease burden but actively promote cellular and molecular longevity.

Limitations and Controversies

Despite compelling evidence linking olive oil consumption to improved health outcomes and longevity, several limitations and areas of controversy should be acknowledged when interpreting the current literature.

Heterogeneity in olive oil types used across studies presents a major challenge. Many observational studies fail to differentiate between EVOO and refined olive oils, which vary significantly in polyphenol content and bioactive potential. EVOO contains over 30 distinct phenolic compounds with known antioxidant and anti-inflammatory properties, whereas refined oils have undergone high-heat and chemical processing that removes most of these constituents [43]. As such, not all olive oil offers equal health benefits, yet this distinction is often blurred in epidemiological assessments and dietary questionnaires.

Measurement error and recall bias in dietary assessments may weaken associations. Many studies rely on self-reported food frequency questionnaires (FFQs), which can lead to under- or overestimation of olive oil intake. Furthermore, FFQs typically do not quantify phenolic content or account for how olive oil is consumed (e.g., raw vs. cooked), both of which influence its biological effects [44].

Another concern is the potential for residual confounding in observational studies. Olive oil intake often coexists with other healthy behaviors and dietary patterns—such as higher consumption of fruits, vegetables, and fish—making it difficult to isolate the specific effects of olive oil. Although multivariate adjustments are common, unmeasured lifestyle factors may still bias results [45].

In clinical trials, limited follow-up durations and surrogate endpoints restrict the ability to assess olive oil's long-term impact on aging. For instance, the PREDIMED study lasted 4.8 years, which is relatively short for assessing outcomes like cognitive decline, frailty, or mortality in aging populations [2]. Additionally, many trials focus on intermediate biomarkers (e.g., LDL oxidation, hsCRP) rather than hard clinical outcomes directly related to aging or longevity.

There is also limited dose-response data available. While higher intake of olive oil is generally associated with greater health benefits, the optimal quantity and frequency of consumption—especially in diverse populations with different dietary baseli-

nes—remain unclear [3]. Moreover, the inter-individual variability in response to olive oil, influenced by genetics, microbiome composition, and metabolic status, has not been sufficiently studied.

Concerns have been raised about mislabeling and adulteration in the commercial olive oil market. Studies have found that some products labeled as “extra virgin” do not meet international chemical or sensory standards, which may compromise reproducibility and real-world applicability of clinical results [46].

Addressing these limitations through standardized phenolic profiling, longer randomized controlled trials, improved dietary assessment tools, and integrative nutrigenomic approaches will be essential for advancing the science of olive oil and aging.

Future Research Directions

Despite the growing body of evidence supporting the role of olive oil—especially EVOO—in promoting healthy aging and disease prevention, several critical gaps remain that warrant further investigation.

Long-term RCTs with aging-specific outcomes are essential to establish causal relationships between olive oil consumption and healthspan extension. While landmark studies such as PREDIMED have demonstrated cardiovascular and cognitive benefits over a median of 4.8 years [2], few trials have assessed endpoints such as frailty, physical function, immune resilience, or multimorbidity in older adults over extended follow-up periods.

There is a need to standardize olive oil phenolic profiling in both epidemiological and clinical studies. The bioactivity of olive oil is strongly influenced by its polyphenol content, which can vary depending on olive variety, harvesting methods, processing, and storage conditions [47]. Developing a robust classification system for EVOO based on phenolic concentration and composition would improve comparability across studies and allow for more precise dose-response analyses.

Nutrigenomic and metabolomic approaches offer promising tools to elucidate how olive oil influences molecular aging pathways. Recent studies suggest that olive oil polyphenols modulate gene expression related to oxidative stress, inflammation, and lipid metabolism [30]. Multi-omics integration—including transcriptomics, epigenomics, and lipidomics—can deepen understanding of the mechanistic effects of olive oil at a systems biology level and help identify new biomarkers of response.

Inter-individual variability in olive oil responsiveness—shaped by genetic polymorphisms, gut microbiota composition, and metabolic status—requires further exploration. For example, polymorphisms in genes such as *SIRT1*, *PPAR γ* , or *Nrf2* may modulate the effect of olive oil on inflammation and oxidative stress [48]. Stratified trials could identify responder subgroups and inform personalized dietary recommendations.

Research is needed on non-Mediterranean and diverse populations, where dietary habits, oil sources, and genetic backgrounds differ substantially. Most existing studies focus on Mediterranean cohorts, limiting generalizability. Cross-cultural trials could help validate the universal relevance of olive oil in aging prevention strategies [49].

Investigations into the synergistic effects of olive oil within whole dietary patterns—such as the Mediterranean or MIND diets—will provide a more ecologically valid understanding of its benefits. Isolating olive oil from its culinary matrix may underestimate its real-world effects when combined with antioxidant-rich vegetables, legumes, and fish.

In summary, advancing olive oil research in aging requires a multidisciplinary approach that bridges clinical nutrition, molecular biology, food science, and personalized medicine. Addressing these directions will enhance the scientific foundation for incorporating olive oil into public health strategies aimed at promoting longevity.

Conclusion

Olive oil—particularly EVOO—emerges as a powerful dietary component with the potential to modulate key biological pathways involved in aging and age-related diseases. Rich in monounsaturated fatty acids and a unique array of bioactive polyphenols, olive oil exerts multifaceted effects on oxidative stress, inflammation, metabolic regulation, and gene expression. Both mechanistic and clinical research supports its role in reducing the risk of cardiovascular disease, type 2 diabetes, neurodegenerative conditions, and certain cancers—major contributors to morbidity in aging populations.

Epidemiological studies consistently associate olive oil consumption with lower all-cause and cause-specific mortality, while clinical trials such as PREDIMED have demonstrated significant cardiometabolic and cognitive benefits. Importantly, emerging evidence suggests that olive oil also influences fundamental hallmarks of aging, including mitochondrial function, cellular senescence, autophagy, and nutrient-sensing pathways such as AMPK, SIRT1, and mTOR.

However, limitations remain, including variability in olive oil composition, methodological heterogeneity, and a lack of long-term aging-specific outcomes. Future research should prioritize standardized phenolic profiling, personalized nutrigenomic investigations, and long-term randomized controlled trials with diverse populations. A systems biology approach integrating omics data with clinical outcomes will be essential to fully elucidate olive oil's role in promoting longevity.

In conclusion, olive oil stands not only as a cornerstone of the Mediterranean diet but also as a functional food with strong potential to enhance healthspan. Its incorporation into dietary patterns represents an accessible, evidence-based strategy to support healthy aging and reduce the burden of chronic disease across the lifespan.

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