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Diet and Age-Related Macular Degeneration: A view on the relationship between dietary patterns, dietary elements supplementation, and Age-Related Macular Degeneration

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ABSTRACT

Age-Related Macular Degeneration (AMD) is a degenerative disorder of the human retina. The pathophysiological essence of AMD is closely related to senescence of retinal tissues and the accumulation of uncleared cellular waste caused by persistent activation of the complement cascade, inflammation, and oxidative stress. It is the main cause of blindness in the population of elders (over 60 years old) in developed countries, and accounts for 6% to 9% of all blindness globally. AMD is a disease associated with multiple risk factors, among which diet has become increasingly popular, being a modifiable one with a potential impact on its treatment and prevention. We conducted a narrative review to summarize current evidence on the relationship between dietary patterns, dietary components, nutritional supplementation and the development and progression of AMD. We observed a strong relationship between a broadly understood diet and risk of AMD. Diet is potentially an important contributor to AMD pathogenesis and a valuable part of its treatment. Evidence suggests that nutrients, such as polyphenols, like resveratrol, carotenoids, especially lutein and zeaxanthin, omega-3 polyunsaturated fatty acids, or the Mediterranean and Oriental dietary patterns, may have a protective effect against AMD. The Western dietary pattern and high intake of omega-6 polyunsaturated fatty acids may increase the risk of AMD progression. Studies on saturated fatty acids remain inconclusive. Considering the fact that there are still inconsistencies in the results, further studies are required for a thorough understanding of this subject and to develop clear nutrition and supplementation strategies for AMD prevention.

Keywords: age-related macular degeneration, diet, dietary pattern, dietary nutrients, AMD.

1. INTRODUCTION

Age-Related Macular Degeneration (AMD) is a degenerative disease of the human eye retina. It is generally localized in the macula lutea, which is a part of the retina with the highest quantity of light-sensitive cells in the human eye. This particular quality makes the macula a key part in clear, sharp, highly detailed, and varied-in-colors vision. The macula conditions the high central visual acuity, as it has the highest density of cones, especially in its central part, the foveola, which is composed almost exclusively of cones (Handa, 2012). The pathophysiological essence of AMD is closely related to senescence of retinal tissues, during which we can observe an accumulation of uncleared cellular waste, which comes largely from retinal pigment epithelium (RPE), at the interface of RPE, Bruch's membrane, and the neurosensory retina. These deposits of cellular debris, called drusen, are composed of lipids, proteins, and carbohydrates. They are usually seen as white or yellowish spots and are frequently the first ophthalmoscopic sign of AMD. Processes underlying this are structural and biochemical changes, such as persistent activation of the complement cascade, inflammation, and oxidative stress (Flores et al., 2021; Pawlowska et al., 2019). There are numerous systems of classification of AMD that differ in their evaluation criteria, especially in non-advanced stages, even though they are usually based on differences in sizes, types, and locations of drusen and pigmentary changes.

In the case of advanced stages of the disease, the criteria are more consistent. The system proposed by the Ferris and Beckman Initiative for Macular Research Classification Committee (Ferris et al., 2013) as a unified clinical classification of AMD suggests three stages of the disease: early, intermediate, and late AMD. The late form is divided into two forms: neovascular AMD (nAMD), commonly called wet AMD, and the atrophic form, described as Geographic Atrophy (GA) and widely referred to as dry AMD. It is important to note that both forms, nAMD and GA, can coincide with each other in the same eye (Flores et al., 2021; Keenan et al., 2021). The main process behind nAMD is choroidal neovascularization (CNV), but neovascular changes such as retinal angiomatous proliferation (RAP) lesions can also occur in the retina.

Vascular endothelial cells and RPE cells proliferation can lead to pigmented epithelial detachment (PED), hemorrhages, and photoreceptor atrophy in the shape of a disciform scar. On the other hand, GA is an atrophy of RPE in the macula, usually accompanied by the thinning of photoreceptors above and the choriocapillaris below. It is called geographic because the confluent loss of RPE forms sharply separated areas with irregular borders that can look like continents. Due to photoreceptor atrophy, we observe severe loss of visual function in affected areas (Keenan et al., 2021). However, in comparison to neovascular AMD, in which the treatment relies on intravitreal injections of inhibitors of vascular endothelial growth factor (anti-VEGF), there are currently no drug therapies available in general clinical practice that can prevent or slow down the development of AMD or restore vision in affected patients (Flores et al., 2021; Keenan et al., 2021). The fact that AMD is affecting such a crucial area makes it an epidemiologically significant cause of vision loss and blindness among adults. Moreover, it is the main cause of blindness in the population of elders (over 60 years old) in developed countries.

Meta-analyses and studies show that it accounts for between 6% and 9% of all blindness globally (Keenan et al., 2021; Wong et al., 2014). The reviews showed that in 2014, about 8.7% of the worldwide population aged 45 to 85 years old suffered from age-related macular degeneration and presented the projected number of people with this disease in 2020 as about 196 million and in 2040 as noticeably increased to about 288 million (Jonas et al., 2017; Wong et al., 2014). Age-related macular degeneration is a disease associated with multiple risk factors, both individual, such as age, genetic and epigenetic changes, and environmental factors, such as sex, ethnicity, iris color, obesity, systemic hypertension, cigarette smoking, sunlight, physical activity, and diet (Keenan et al., 2021).

Recently, diet has become an increasingly popular topic among researchers. Nevertheless, the majority of current analyses are conducted based on several years-old but still some of the most valuable studies in this area, which are: "Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8." (AREDS1) (Age-Related Eye Disease Study Research Group, 2001) and "Age-Related Eye Disease Study 2 Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: The age-related eye disease study 2 (AREDS2) randomized clinical trial." (Chew et al., 2013). In AREDS1, we can find conclusions that antioxidant vitamin supplementation may be beneficial for individuals suffering from AMD (Age-Related Eye Disease Study Research Group, 2001).

However, another study conducted by Evans & Lawrenson (2017) shows that even though correct supplementation might be beneficial, it does not prevent the primary onset of AMD. Authors emphasize that diet is a very broad term that can be examined through its numerous aspects, such as dietary patterns, single or multiple food items, different nutritional components of food (Chapman et al., 2019), and individual element supplementation (Age-Related Eye Disease Study Research Group, 2001). In the context

of dietary patterns for this study, we distinguish ones like the Mediterranean diet, the Western diet, and the Oriental diet. Considering the food items and separate nutritional elements, researchers focus on ones like: fruits and vegetables; nuts; fish and seafood; red meat; alcohol; dairy; eggs; grains; omega-3 polyunsaturated fatty acids (omega-3 PUFAs) like α -linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA); omega-6 polyunsaturated fatty acids (omega-6 PUFAs) specifically arachidonic acid and eicosadienoic acid; monounsaturated fatty acids (MUFA) like oleic acid (OA); saturated fatty acids (SFA); carotenoids like lutein, zeaxanthin, α -carotene and β -carotene; α -tocopherol; quercetin; vitamin D; vitamin C; zinc; calcium; carbohydrates; cholesterol; dietary nitrates.

Taking into account that most people's diets are very restricted to a single food or even a single dietary pattern, for the huge majority of them, the diet varies seasonally or periodically due to personal preferences, it is almost impossible to demonstrate precisely the complexity of the correlation between diet and age-related macular degeneration. Since current treatments for AMD, especially in its late stage with predominant GA, remain so limiting that they prevent medical professionals from successfully suspending the progression of the disease and restoring vision in patients with severe loss, it is important to address the factors that increase the risk of AMD. For that reason, a systematized knowledge about the impact of diet and nutritional interventions on AMD might be a valuable part of the therapy of AMD, provided not only by ophthalmology specialists but also by general practitioners.

The aim of this narrative review is to summarize current evidence concerning the relationship between dietary patterns, dietary components, nutritional supplementation, and the development and progression of age-related macular degeneration (AMD).

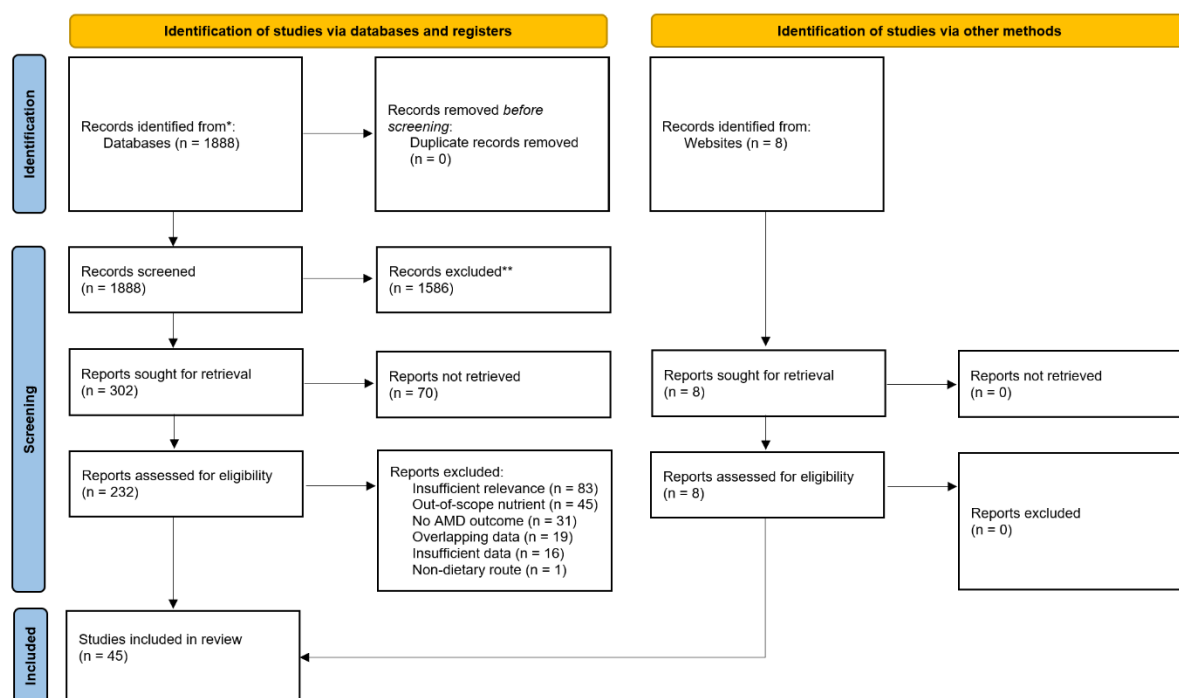


Figure 1. PRISMA flow diagram.

2. REVIEW METHODS

We performed a non-systematic literature search using the PubMed/MEDLINE database for studies published from 2013 up to March 2026. In the search used combinations of Medical Subject Headings (MeSH) and free-text terms such as "age-related macular degeneration", "AMD", "diet", "dietary patterns", "nutrition", "dietary supplements", "AREDS", "AREDS2", "fatty acid", "omega-3 fatty acids", "antioxidants", "lutein", "zeaxanthin", "polyphenols", "Mediterranean diet", "vitamin C", "vitamin E", "vitamin D", "resveratrol", and "zinc". We manually screened the reference lists of relevant articles to identify further search terms and other relevant publications. All the records found were screened through PubMed together with the database search results. Therefore, all studies that we included were identified via the PubMed/MEDLINE database. The main inclusion criterion was investigating adult populations with AMD. Studies were also included if they evaluated dietary patterns, food groups, nutrients, nutritional biomarkers, or dietary

supplementation in relation to AMD risk, progression, or visual outcomes. We qualified various study designs as suitable for our review, among which randomized controlled trials, cohort, case-control, and cross-sectional studies, but also meta-analyses and similar systematic reviews can be found. We excluded publications that were not related to nutrition and AMD, animal studies without a human component, or studies focusing on other ocular diseases. We did not include conference abstracts, editorials, letters, errata, case reports or unpublished reports (including preprints), which were unsuitable for our study. Finally, we rejected studies in languages other than English, duplicate records, and articles with insufficient relevant outcome data or methodological information. After performing the research, we extracted necessary data on population characteristics, dietary exposures, classification of AMD, and main study outcomes. 37 of 46 references cited in this review were identified through the PubMed/MEDLINE search described above. The remaining 8 references provided disease background, classification, and epidemiological context and were included in the PRISMA flow diagram as references identified via other methods. Due to divergence in study designs, dietary assessment methods, and reported outcomes, we summarized the results in a narrative review format. The article screening process followed the PRISMA guidelines (Figure 1).

3. RESULTS AND DISCUSSION

Polyphenols

Dietary polyphenols are biologically active chemicals with phenolic structure features that can often be found in food and vegetables, but also in beverages such as tea, chocolate, and wine. They are widely distributed in nature as a group of chemical compounds that, due to their diversity, are categorized using different criteria like origin, biological function, and chemical structure. Based on them, we can distinguish: phenolic acids (benzoic acid and cinnamic acid), flavonoids (isoflavones, neoflavanoids, chalcones, flavones, flavanols, flavanones, flavanonols, proanthocyanidins, and anthocyanidins), and polyphenolic amides (Tsao, 2010). Dietary polyphenols present many beneficial effects for human health, among which we can find anticancer, anti-inflammatory, antiapoptotic, and antioxidant activities. Those effects occur thanks to various mechanisms, among which one of the most significant is their intensive antioxidant activity. That activity is a natural defense mechanism against oxidative stress, which is significantly linked to the development of various diseases, including AMD (Pawlowska et al., 2019). Among many polyphenols, we can bring forward ones that are potentially important for human health, like resveratrol, curcumin, quercetin, and hydroxytyrosol.

Resveratrol, which is one of the best-studied phytophenols with pleiotropic properties due to its well-recognized antioxidant activity, shows the ability to protect the RPE cells from oxidative stress that can damage them and cause their apoptosis. Resveratrol, used in preventive therapy, promotes an increase in the activity of several enzymes that take part in antioxidant defense, such as superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase. Besides that, resveratrol tends to increase the level of reduced glutathione synthesized by cells to be a natural endogenous antioxidant. And what is more, it expresses the ability to inhibit the generation of reactive oxygen species (ROS) by RPE cells and also may have the ability to directly scavenge free radicals (Dziedziak et al., 2021; Lançon et al., 2016). Therefore, we can observe that it takes its role both intracellularly and extracellularly. In a study presented by Datseris et al., (2025), a statement is posed that resveratrol may have the ability to modulate inflammatory processes.

The modulation is achieved by inhibiting the secretion of VEGF-A and -C previously induced by inflammatory cytokines, the transformation of the growth factor- β (TGF- β), and hypoxia through interfering with the PI3K-AKT-mTOR and NF- κ B pathways. The study exposed the fact that oral supplementation of Resvega, an oral supplement containing resveratrol and omega-3 fatty acids, prevented the progression of AMD, which was observed as a significantly lower number of intravitreal injections of anti-VEGF agents over an 18- and 24-month period (Datseris et al., 2025). In their study on resveratrol, researchers also report that its impact on inflammatory mechanisms includes down-regulation of COX-1 and COX-2 activity in a dose-dependent manner and Intercellular Adhesion Molecule-1 (ICAM-1) and Monocyte Chemoattractant Protein-1 (MCP-1) production, which are decisive in the direction of the inflammatory process (Lançon et al., 2016).

Curcumin is a strong antioxidant derived from turmeric (Tsao, 2010). It was shown that curcumin increased the viability of ARPE-19 cells, which were under conditions of aging stimulated by the addition of H₂O₂. Curcumin tended to inhibit apoptosis in ARPE-19 in both early and late stages by upregulation of the antiapoptotic BCL2 (B-cell CLL/lymphoma 2) protein and downregulation of the proapoptotic proteins BAX (BCL2-associated X) and CASPASE-3. Moreover, it takes part in the regulation of multiple oxidative stress biomarkers like malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione transferase (GSH). Curcumin also shows a protective effect against the cytotoxicity of acrolein, which is a chemical substance found in cigarettes, in ARPE-19 cells, dependent on the activation of NRF2. NRF2 is a factor that controls transcription of several genes, including ones that account for antioxidant defense,

cellular waste clearing, DNA damage response, and detoxification. Preincubation of RPE cells that showed features of AMD with curcumin and H₂O₂ (added to induce cell death) was followed by reduced levels of ROS and apoptosis. Those processes were linked with higher expression of the antioxidant genes HO-1 (heme oxygenase 1), another enzyme whose activation plays a significant role in the retinal protective reaction to oxidative stress, and SOD2 (superoxide dismutase 2). On the other hand, curcumin elevated mRNA levels of PDGF, VEGF, and IGFBP-2, which are critical factors in the progression of AMD (Pawlowska et al., 2019). Just as resveratrol, curcumin also inhibits COX-1 and COX-2 activity (Lançon et al., 2016).

Quercetin is a compound belonging to the flavonol subgroup of flavonoids (Tsao, 2010) and occurs plentifully in apples, onions, and berries (Kim et al., 2018). It presents a protective effect against oxidative stress and inflammation in the retina through multiple pathways. Similarly to curcumin, quercetin regulates the transcription of genes influencing mechanisms of apoptosis like BCL2, BAX, and CASPASE-3, in ARPE-19 cells subjected to oxidative stress caused by hydrogen peroxide, but also induces the expression of NRF2 along with HO-1, and leads to lower levels of ROS in the retina (Pawlowska et al., 2019).

The last-mentioned polyphenol is hydroxytyrosol. It is a polyphenol encountered in olive oil, whose higher weekly intake was connected to a lower prevalence of late AMD. Hydroxytyrosol, thanks to its antioxidant activities, prevents LDL-cholesterol from oxidation, and, similar to other polyphenols, it reduces the expression of inflammatory mediators. In *in vitro* studies, hydroxytyrosol showed a protective effect against oxidative damage in RPE cells (Cougnard-Grégoire et al., 2016).

Carotenoids

Carotenoids belong to the xanthophyll family (Arunkumar et al., 2018), are a valuable part of the vast antioxidant defense system of the retina (Carneiro & Andrade, 2017), and, what is more, they are usually considered the most important ones (Pawlowska et al., 2019). There are about 750 carotenoids identified in the natural environment. About 40 of them were noticed in the examination of human food, and 15 of them were found in human cells and tissues. However, just two of them, specifically lutein, zeaxanthin, and their metabolites, are naturally observed in retinal cells. They are diversely distributed in the retina, with the highest concentration in the macula (Arunkumar et al., 2018). Zeaxanthin localizes predominantly in the fovea, and lutein has a higher concentration in the peripheral region (Arunkumar et al., 2018; Carneiro & Andrade, 2017). High levels of both carotenoids in the macular area are also responsible for its unique color (Dziedziak et al., 2021). The lutein to zeaxanthin ratio is 1:2.4 in the center and over 2:1 in the peripheral areas of the human retina (Arunkumar et al., 2018). Main dietary sources of lutein and zeaxanthin in the human diet are green leafy vegetables like spinach, parsley, kale, lettuce, broccoli, zucchini, orange-yellow fruits like orange, tangerine, papaya, mango, and animal products like egg yolk (Arunkumar et al., 2018; Dziedziak et al., 2021; Walchuk & Suh, 2020). Both carotenoids are lipophilic nutrients. After ingestion, carotenoids are absorbed by enterocytes and packaged into chylomicrons. In this form, they are transported through the body with other lipid-soluble nutrients (Walchuk & Suh, 2020). Their function in protecting the RPE cells is closely linked to their antioxidant characteristics. Carotenoids can scavenge free radicals but also have a unique ability to absorb blue light, which reduces the amount of ROS generated in the light-activated oxygenation and, by that, induces oxidative stress and degeneration of RPE cells (Carneiro & Andrade, 2017; Dziedziak et al., 2021; Feng et al., 2019). Epidemiological studies often support the thesis that patients with lower concentrations of serum carotenoids and MPOD are at a higher risk of developing AMD (Arunkumar et al., 2018).

Previously conducted studies show that carotenoid supplementation may have a beneficial effect in AMD through significant improvement in macular pigment optical density (MPOD), and thus improving visual performance in patients with AMD (Feng et al., 2019; Walchuk & Suh, 2020) and prevention of the onset of the disease (Carneiro & Andrade, 2017). The beneficial effects of carotenoids are even stronger when their supplementation is incorporated into other antioxidant interventions and combined with a healthy lifestyle (Carneiro & Andrade, 2017). Most clinical studies investigate the joint impact of lutein and zeaxanthin supplementation on retinal health because of their common affiliation to the carotenoid group, similar chemical properties, simultaneous occurrence in the human retina, and common distribution in food products. Also, they are supplemented together because lutein absorption is dependent on zeaxanthin presence (Mrowicka et al., 2022). While most *in vitro* studies were very promising, the results of epidemiological studies are inconclusive. The majority of analyses show that concurrent, prolonged supplementation of various doses of lutein and zeaxanthin daily for periods of 9 months to 3 years results in higher concentrations of the mentioned carotenoids in serum and a significant increase in MPOD in comparison to placebo groups. Unlike the improvement in MPOD measurements, which was observed in the vast majority of studies, the vision improvement was observed only in several studies in the form of increased visual acuity and enhanced contrast sensitivity (Walchuk & Suh, 2020).

In opposition to many promising works, the major study AREDS2 ended up with conclusions that supplementation of different variants of the formulation of lutein + zeaxanthin and DHA + EPA showed no statistically significant overall effect on progression to advanced dAMD or changes in visual acuity in studied patients. There was no beneficial or harmful effect of the supplementation in the case of treatment of advanced AMD. Yet, the study showed that lutein + zeaxanthin might be a better choice for supplementation in a population of smokers (Chew et al., 2013). The analysis performed on a nutrition examination survey conducted among older women in Korea also did not find a relationship between AMD and the supplementation of carotenoids (Kim et al., 2018). The results of an analysis presented by Feng et al., (2019) support the thesis that supplementation of lutein (10 mg or 20 mg per day) for longer than 6 months leads to higher MPOD in both supplemented without and with other carotenoids. Only a part of the clinical trials was connected with better visual acuity and higher contrast sensitivity. Higher consumption of green vegetables, which are usually a good source of lutein and zeaxanthin, can be a significant protection against the onset of late AMD. Regular intake of antioxidants in higher doses, especially lutein and zeaxanthin, can noticeably reduce early AMD associated with genetic risk factors (Mrowicka et al., 2022). There were considerably lower levels of β -carotene observed in individuals with neovascular AMD in comparison to a control group of patients, which led researchers to deduce that higher intake of β -carotene in a diet can contribute to reduced risk of neovascular AMD (Aoki et al., 2016).

Another study based on the National Health and Nutrition Examination Survey in Korea examined the prevalence of AMD in the population of smoking older men, aged ≥ 65 years. The study displayed noticeable inverse associations between fruits and vegetables and antioxidant nutrients (including lutein/zeaxanthin and β -carotene) intake and AMD. Researchers drew the conclusion that fruits and vegetables, α -carotene, and β -carotene may have protective value against AMD in elderly male smokers (Kim et al., 2017). The same relationship between carotenoids and nAMD was spotted by clinicians in the Hong Kong Chinese population. Significantly lower levels of carotenoids were observed in AMD subjects compared to controls. The odds ratio of having AMD for each of them was calculated as 2.78 for beta-carotene, 6.02 for lycopene, and 4.82 for combined lutein and zeaxanthin (Ng et al., 2019).

Fatty acids

Fatty acids (FAs) are known to be, among proteins and carbohydrates, a cardinal nutritional component of a human diet. They are known to have a large influence on human health and to take part in the pathogenesis of many diseases. They do play an important role in the pathogenesis of ophthalmological diseases, as the retina is one of the richest tissues in lipids in the human body. FAs play major roles in the human body, amongst which can be mentioned building cell membranes or being a source of energy. Fatty acids are categorized based on the length of their carbon chain, presence of double bonds in them, and location of the first double bond relative to the terminal methyl group. Using this classification, we can distinguish saturated fatty acids (SFAs), monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs). SFAs do not have double bonds at all. MUFAs like oleic acid (omega-9 fatty acid – fatty acid with a double bond on the 9th carbon) have one double bond, and PUFAs contain more than one double bond in their structure. Polyunsaturated fatty acids can be grouped into 2 groups.

Omega-3 PUFAs have a double bond located on the 3rd carbon, and omega-6 PUFAs have a double bond located on the 6th carbon (Bisen & Singh, 2025). Docosahexaenoic acid (DHA), α -linolenic acid (ALA), and eicosapentaenoic acid (EPA) belong to omega-3 PUFAs, which are the most important PUFAs for human health. All of them are part of one metabolic pathway in which DHA can be synthesized from EPA and EPA can be synthesized from ALA (Ng et al., 2019). Due to a lack of a specific enzyme, the human body cannot synthesize PUFAs, so they have to be provided with a diet. Among major omega-6 fatty acids, we can find linoleic acid (LA), which is a precursor to all omega-6 FAs in the human body, arachidonic acid (AA), and docosapentaenoic acid (DPA). Fatty acids are essential for the human eye, as in the retina PUFAs account for 45% of its phospholipids, SFAs account for 37%, and MUFAs stand for 10% of them (Bisen & Singh, 2025). While omega-3 PUFAs present anti-inflammatory properties, omega-6 PUFAs are precursors of pro-inflammatory eicosanoids (Ng et al., 2019).

High PUFA content, especially DHA, which accounts for almost 60% of PUFAs in other segments of photoreceptors of the retina, and a constant turnover of outer segment membranes compel a persistent supply of DHA and its precursors like EPA with diet. Main sources of omega-3 FAs in the human diet are fatty fish, eggs, nuts, and particular vegetables (Lawrenson & Evans, 2015). DHA and EPA have pleiotropic effects using mechanisms like gene expression regulation, signal transduction, and changes in plasma membrane dynamics. Both of these PUFAs have positive effects on human health, including protective potential against age-related eye diseases. Those effects come from the ability of PUFAs to modulate inflammatory pathways. The modulation proceeds through reducing the production of pro-inflammatory eicosanoids, cytokines, and reactive oxygen species, but also through changes in gene expression. The

anti-inflammatory properties may also inhibit neovascularisation. As omega-3 fatty acids play an important role in retinal membrane regeneration, a lack of them can lead to an imbalance in retinal lipids, which causes debris accumulation and the formation of drusen (Carneiro & Andrade, 2017). Those biological properties led scientists to the hypothesis that DHA and EPA have a protective effect and are linked to the incidence of AMD.

In a prospective study by Wu et al., (2017a) based on over a hundred thousand individuals, researchers measured a cumulative individual intake of DHA and EPA from diet, using a validated food frequency questionnaire. The study had a 24- to 28-year follow-up on participants, calculating their daily intake of DHA and EPA based on fish and seafood consumption and fish oil-based supplement intake. Among participants, they confirmed 1589 intermediate and 1356 advanced AMD cases. The study shows an inverse correlation between intake of omega-3 FAs in the diet and risk of visually significant intermediate AMD. The risk was 17% to 40% lower for patients with higher intake of omega-3 FAs. Moreover, long-term supplementation of fish oils, which on average contain 590 mg of EPA + DHA, may also have a protective value against intermediate AMD. Although the results of this study were not consistent in the case of advanced AMD, and did not show a protective effect against the late stage of AMD explicitly.

An inverse relationship between high intake of omega-3 fatty acids and AMD was also shown in a study conducted by Aoki et al., (2016) in Japan. They analyzed the influence of the intake of omega-3 PUFAs, which was higher than in other studies in Japanese patients. The average daily dose of consumed omega-3 FAs in this study was approximately 3.2g. The study suggested that even such a high intake of omega-3 FAs is associated with a lower incidence of neovascular AMD. In a meta-analysis conducted by Zhong et al., (2021), taking into account the intake of fatty acids and their concentration in plasma, researchers analyzed the incidence of AMD in different groups of patients. In the case of overall PUFAs and ALA, there was no evidence of a non-linear association between their intake and risk of AMD. On the other hand, considering DHA and EPA intake and levels, the study showed a strong relationship between DHA and EPA and risk of early AMD, but no association with risk of advanced AMD. Furthermore, their analysis showed that in the case of early AMD, the dose of DHA and EPA was directly associated with a reduction in the risk of disease. For each 1g per day increase in dietary intake, the risk of early AMD was reduced 33% for DHA and AMD combined, 50% for DHA, and 60% for EPA. Results of the trials analyzing the effect of omega-3 FAs are not consistent. The AREDS2 study, which was the addition of lutein (10 mg) + zeaxanthin (2 mg) and DHA (350 mg) + EPA (650 mg) to the original AREDS formulation, consisted of antioxidant supplementation in AMD. While ARDES1 results were associated with a 25% reduction of the risk of developing advanced AMD at 5 years, the ARDES2 formulation, including the addition of DHA and EPA in one of the subgroups to the original formulation, showed no statistically significant further reduction of the risk of progression to advanced AMD or visual acuity (Chew et al., 2013).

A similar conclusion was drawn in an observational study by Christen et al., (2020) based on the cohort of the Vitamin D and Omega-3 Trial (VITAL), a randomized clinical trial of 25,871 adult US men and women, designed initially to investigate the role of vitamin D and omega-3 FAs in preventing cancer and cardiovascular diseases. The supplementation of omega-3 FAs consisted of daily supplementation of 1 g of EPA + DHA in a ratio of approximately 1.2:1, for a median of 5.3 years. The analysis ultimately evaluated the HR of AMD as 0.93 for incident AMD and 1.05 for AMD progression, thereby showing no statistically significant effect of DHA and EPA supplementation on the reduction of the risk of AMD. In a different study, Wu et al., (2017b) analyzed the intake of α -linolenic acid in the diet and risk of AMD. Researchers found that high intake of ALA was connected with an increased risk of intermediate AMD, but only in the period before 2002 and not after that. In contrast, they did not find any significant association of ALA intake with advanced AMD in any period of time. Lower levels of omega-3 PUFAs, in comparison to healthy participants, specifically EPA and DHA, were also found in subjects with AMD in a study on Hong Kong adults. For those individuals, the odds ratio of developing AMD was increased by 6.33 for DHA, 7.79 for EPA, and 3.11 for ALA (Ng et al., 2019).

As mentioned before, omega-6 PUFAs have, opposite to omega-3 PUFAs, a pro-inflammatory effect by being a source of pro-inflammatory eicosanoids and competing with omega-3 PUFAs in the metabolic pathways (Bisen & Singh, 2025). Omega-6 PUFAs are found in large quantities in foods like meat and dairy (Ng et al., 2019); therefore, they are widely prevalent in a Western diet (Bisen & Singh, 2025). In a previously mentioned case-control study, researchers analyzed how levels of omega-6 and omega-3 PUFAs, among other nutrients, affect the risk of exudative AMD development in the same population of Hong Kong adults with a Chinese diet. They found significantly higher levels of omega-6 PUFAs, like arachidonic acid and eicosadienoic acid, in subjects with AMD. Also, low levels of arachidonic acid were found to be protective in the case of AMD (Ng et al., 2019). Ng and Leung used the same population of Chinese adults to expand the scope of the study of the relationship between PUFA levels and the risk of developing exudative AMD.

In another study, they analyzed the omega-6/omega-3 PUFAs ratio, levels of its lipid peroxidation products (LOP), which are generated in the process of PUFAs oxidation under conditions of oxidative stress, and antioxidant status, considered as the activity of

glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT). Researchers considered upregulation of SOD and CAT in AMD patients as a determinant of oxidative stress. The omega-6/omega-3 PUFAs ratio was higher in individuals with AMD than in healthy participants, presented as 8:1 in the healthy group and 11:1 in the AMD group, so it was approximately 35% higher than in healthy controls. The levels of SOD and CAT were significantly higher in the AMD group than in the healthy group. On the other hand, there was no visible difference between the two groups in GSH levels. The study also showed that the plasma levels of omega-6 PUFA LOPs were significantly higher, and omega-3 LOPs were consistently lower in the group of patients with AMD. It is important to note that LOPs generated in PUFA peroxidation are biologically active and involved in the inflammatory response. The study ended up with the conclusion that a high omega-6/omega-3 PUFAs ratio led to upregulation of pro-inflammatory omega-6 PUFAs LOPs and downregulation of anti-inflammatory omega-3 PUFAs oxidation metabolites, which increased the odds ratio of developing exudative AMD (Leung et al., 2019).

Saturated fatty acids (SFAs) are the second most common group of phospholipids in the retina (Bisen & Singh, 2025). The results of studies on the connection between SFAs and AMD are very inconsistent. The study conducted by Sasaki et al., (2020) analysing the relationship between SFAs intake and early AMD in participants of the Tsuruoka Metabolomics Cohort Study showed reduced risk of early AMD development in individuals with increased SFAs intake among subjects with very low SFAs intake. Individuals in the highest quartile of SFAs intake have an odds ratio of early AMD of 0.71 compared to individuals in the lowest quartile of SFAs intake. Another study on the Japanese population, published by Yusukawa et al., (2023), showed a similar correlation. In a group of men, especially those with increased SFAs intake, scientists recognized a significantly reduced prevalence of any type of AMD. They did not find a similar correlation in the women's group. Moreover, they observed trends for decreasing odds ratios of developing AMD, which were connected with increasing SFAs intake. In contrast to the Japanese population, in the Chinese population described by previously mentioned scientists in their study, high levels of SFAs, like palmitic acid and pentadecylic acid, were associated with an increased risk of having AMD. The odds ratio, comparing the top to the bottom quartile, when calculated individually for palmitic acid was 11.48, and for pentadecylic acid was 33.75 (Ng et al., 2019).

Diet type

Diet is one of the modifiable behavioral risk factors that play an important role in the development of various diseases (Gastaldello et al., 2022). It is an important factor because, unlike others, such as genetics, age, or sex, it presents a potential area for intervention in the therapeutic process (Gourgouli et al., 2023). Diet can be considered and studied in various ways, such as single or multiple nutrient intake, single or multiple food items consumption, or different dietary patterns (Chapman et al., 2019). The majority of studies focus on researching the association of individual nutritional components, single food items, or micronutrients and macronutrients with the onset and progression of age-related macular degeneration. Considering mutual interactions between several nutrients and effects of groups of foods, it is important to consider diet as a wider concept of dietary pattern (Francisco et al., 2020). Therefore, nowadays researchers more often tend to investigate the relationship between AMD and overall diet or particular dietary patterns rather than single nutritional compounds (Chiu et al., 2014; Francisco et al., 2020; Gourgouli et al., 2023; Sasaki et al., 2022). Analyzing diets, we can distinguish three major dietary patterns: the Mediterranean dietary pattern (Gastaldello et al., 2022), the Western dietary pattern, and the Oriental dietary pattern (Chiu et al., 2014).

The Mediterranean dietary pattern (Med diet) is a traditional diet for residents of the Mediterranean countries such as Italy, Greece, and Spain. The diet is mostly plant-based, and consequently rich in antioxidants thanks to the high content of vegetables, fruits, whole grains, beans, seeds, nuts, and spices. This diet is rich in MUFAs present in olive oil, which is an important part of it. Furthermore, moderate consumption of fish provides omega-3 PUFAs to the body. Another characteristic feature of the Med diet is low consumption of dairy, red, and processed meat. It is considered one of the most beneficial diets for human health. Consistent adherence to this dietary pattern is known for its ability to reduce overall mortality and the incidence of various diseases (Gastaldello et al., 2022). Adherence to the Med diet is often evaluated using a system for that purpose, which is the Mediterranean Diet Score (MDS). The MDS is based on the consumption of key factors such as vegetables, fruits, legumes, cereals, fish, meat, dairy products, alcohol, and the MUFAs-to-SFAs ratio (Merle et al., 2019).

There are multiple studies that analyse the beneficial effect of adherence to the Mediterranean diet on the progression of AMD. In a study based on Dutch and French populations of almost 5000 participants by Merle et al., (2019), the researchers showed that for both populations, higher adherence to MDS was connected with a lower incidence of advanced AMD. No association was found between adherence to MDS and incidence of neovascular AMD. However, in the pooled data analysis, it was significantly connected with

incident advanced AMD, causing a 41% risk reduction of incident advanced AMD. Patients with greater adherence to the Med diet, described as an alternate Mediterranean score of 6 and higher, presented a reduced risk of progression to advanced AMD in a study on a population of Greeks. Authors showed that the likelihood of progression to advanced AMD was 25% lower in these patients (Merle et al., 2015). Gourgouli et al., (2023) and fellow scientists investigated the synergistic effect of the Med diet and nutritional supplementation based on the ARDES2 formula. In their study, they presented a positive correlation with slowing AMD progression. High adherence to the Med diet resulted in a 2.2 times higher likelihood of slowing AMD progression compared to those with low adherence. In the case of nutritional supplementation, patients who received supplementation had an 8.2 times greater chance of slowing the progression of AMD. Moreover, the results showed that the patients who simultaneously had high adherence to the Med diet and had active supplementation had a 24.5 times higher likelihood of slowing AMD progression in comparison to patients who did not follow both recommendations. Hogg et al., (2017) in the European Eye (EUREYE) Study investigated the effect of diet on adults with and without AMD from 7 European countries. The study showed that increasing MDS was inversely related to the odds of having neovascular AMD. Participants with MDS of 6 or higher have approximately a 50% reduced adjusted ratio of developing neovascular AMD. However, no significant association between MDS and early AMD was found in the study.

In opposition to healthy dietary patterns like the Mediterranean Diet, we can put the Western Diet. The Western dietary pattern is usually characterized by higher intakes of red meat, saturated fats, highly processed foods, sweets and desserts, and sugar-sweetened beverages. The Western-style diet is marked by low fiber and high simple sugar and starch intake, which leads to increased intestinal inflammation, increased gut permeability, and microbial translocation, resulting in decreased resilience to enteric infections. For many scientists, the Western-style diet is connected to an increased risk of AMD (Francisco et al., 2020). Chiu et al., (2014) evaluated major American dietary patterns, creating a factor score for each pattern, constructed by summing observed intakes of the component food items and using a specific matrix. They found that higher adherence to the Western dietary pattern resulted in higher odds of both early and advanced AMD. The odds ratio per Western score unit increase was 1.15 for early and 1.55 for advanced AMD. The increase in odds between the group with the highest adherence to the Western Diet in comparison to the group with the lowest adherence to the Western Diet was almost 60% for early AMD, and almost three times for advanced AMD.

Amirul Islam et al., (2014), using data collected in The Melbourne Collaborative Cohort Study, identified a dietary pattern similar in characteristics to the Western dietary pattern, and called it Factor 4 - "red meat". They found that Factor 4 was associated with a higher prevalence of advanced AMD. For participants born in Australia/New Zealand/United Kingdom, Factor 4 above the median was connected with an odds ratio of 1.46 of advanced AMD. In a study on the association of dietary patterns and AMD in the multiethnic older Singaporean population, Zhang et al., (2026) presented three dietary patterns. The "snacks, fried foods, and refined carbohydrates" pattern can also be considered a Western dietary pattern thanks to the characteristics of its food elements. The study suggested that higher adherence to the pattern was directly associated with higher odds of developing early AMD (OR = 1.63). Yet, no substantial association was found with late AMD.

The other dietary pattern identified by Chiu et al., (2014) in a study on major American dietary patterns was the Oriental dietary pattern. The Oriental dietary pattern is characterized by higher intake of vegetables, legumes, fruit, whole grains, tomatoes, and seafood. The scientists found in their study that a higher Oriental pattern score, based on specific food intake, was strongly connected to lower odds for both early and advanced AMD. The odds ratio per Oriental score unit increase was 0.90 for early AMD and 0.73 for advanced AMD. When comparing individuals with the highest adherence to the Oriental pattern to individuals with the lowest adherence, there was cumulatively about a 30% reduction in the odds of early AMD and more than a 60% reduction in the odds of advanced AMD.

In another study, Chiu et al., (2017) described three minor dietary patterns overlapping with the Oriental dietary pattern and associated with the prevalence of advanced AMD: the breakfast pattern, the Caribbean pattern, and the salad pattern. Adherence to the breakfast pattern, consisting of cold breakfast cereal, whole grains, and fruits, was connected with at least a 26% to 42% reduction in the prevalence of advanced AMD. As well, adherence to the Caribbean pattern, characterized by poultry, fish and seafood, rice, low-fat dairy, and organ meat consumption, resulted in approximately a 35% decrease in the prevalence of advanced AMD. Lastly, the salad pattern, composed of tomatoes, green leafy vegetables, and salad dressings, was not significantly associated with the prevalence of AMD.

Discussion

This review study analyzed and gathered knowledge on the impact of various dietary factors on the prevalence and progression of age-related macular degeneration. We analyzed multiple studies investigating the association of several nutrients, food items, and diets with AMD. We observed a strong relationship between broadly understood diet and risk of AMD. Particular nutrients, food ingredients, and dietary patterns can reduce or increase the risk of outcome and progression of age-related macular degeneration. Table 1 summarizes the results of the article, showing the main findings and direction of association of dietary factors with AMD.

The reviewed evidence suggests that polyphenols present in the human diet may have a protective effect against AMD. The key factor in their effect is the impact on the main mechanisms of AMD pathogenesis, such as oxidative stress, inflammation, and apoptosis. Resveratrol, curcumin, quercetin, and hydroxytyrosol show consistent ability to protect RPE and suppress the pro-inflammatory mediators. Among them, resveratrol has the most promising evidence so far. Early clinical studies suggest it may help slow the progression of AMD when included in combination supplements (Datseris et al., 2025). Most of the current data come from in vitro and preclinical studies. Clinical evidence is still limited because of small sample sizes, different study designs, and the low bioavailability of some polyphenols. To better understand their long-term effects, best dosing, and role in preventing and managing AMD, well-designed randomized clinical trials are needed.

Currently available data show that carotenoids such as lutein and zeaxanthin, which are commonly found in the human retina due to their antioxidant and blue-light filtering properties, play a significant role in protecting the eye against AMD (Carneiro & Andrade, 2017; Dziedzic et al., 2021; Feng et al., 2019). Lower dietary carotenoid levels were often observed in individuals with AMD (Kim et al., 2017; Ng et al., 2019). Even though supplementation consistently elevates the concentration of carotenoids in the serum and MPOD, its impact on visual acuity and the progression of age-related macular degeneration is still not consistent across clinical studies. A limited overall benefit has been demonstrated in some studies, including large clinical trials such as AREDS2 (Chew et al., 2013; Kim et al., 2018). The observed inconsistencies may be caused by differences in the design of the studies, supplementation protocols, disease stage, genetic background, and lifestyle factors.

On the other hand, current evidence supports the fact that the presence of carotenoid-rich foods in the diet and maintaining a healthy lifestyle may potentially reduce the risk of AMD and promote better visual acuity (Carneiro & Andrade, 2017; Feng et al., 2019; Walchuk & Suh, 2020). Further studies are necessary for a better understanding of the subject. It is essential to identify populations most likely to benefit from carotenoid supplementation and to establish optimal dosing strategies.

Specific types of fatty acids may influence the development and progression of age-related macular degeneration (AMD), although current findings are inconclusive. Omega-3 fatty acids, especially docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), have been linked to protection against early and intermediate age-related macular degeneration (AMD) because of their anti-inflammatory, antioxidant, and neuroprotective properties (Aoki et al., 2016; Wu et al., 2017a; Zhong et al., 2021). However, evidence from randomized clinical trials remains inconclusive regarding the efficacy of omega-3 supplementation in preventing progression to advanced AMD (Wu et al., 2017b). The opposite effect is frequently associated with high intake of omega-6 FAs or an elevated omega-6/omega-3 FA ratio. These properties resulted in a greater risk of age-related macular degeneration by leading to increasing inflammation and oxidative stress (Bisen & Singh, 2025; Leung et al., 2019; Ng et al., 2019). In the case of SFAs, studies have concluded with non-coherent results.

In Japan, in particular in the population of men with higher SFAs, a lower risk of early AMD was observed (Sasaki et al., 2020; Yasukawa et al., 2023). The opposite effect was observed in the Chinese population, in which higher levels of specific SFAs, including palmitic acid and pentadecylic acid, were strongly connected with an increased risk of AMD (Ng et al., 2019). However, this inconsistency shows that other variables, including overall diet, disease stage, ethnicity, and individual differences in metabolism, may affect patient outcomes. Additional long-term studies and clinical trials are needed to formulate the optimal composition of dietary fats and create clear nutrition-based strategies for AMD prevention and management.

Increasing evidence suggests that overall dietary patterns offer a more comprehensive understanding of dietary influences on AMD. In general, diets rich in vegetables, fruits, whole grains, legumes, seafood, and other nutrient-dense foods are associated with a lower risk of AMD. Among these, the Mediterranean diet has shown the strongest and most consistent protective association. High adherence to this dietary pattern is associated with a lower risk of advanced and neovascular AMD, reduced disease progression (Hogg et al., 2017; Merle et al., 2015, 2019), and may act synergistically with AREDS2 nutritional supplementation to further enhance protective effects (Gourgouli et al., 2023). The Oriental dietary pattern exhibited a strong inverse association with the risk of both early and advanced AMD (Chiu et al., 2014). Other overlapping minor dietary patterns, including the breakfast and the Caribbean patterns,

were similarly connected with a reduced prevalence of advanced AMD (Chiu et al., 2017). These results suggest that plant-based diets that include regular seafood consumption can lower the risk and progression of AMD. On the other hand, the Western dietary pattern is associated with an increased risk of age-related macular degeneration (Francisco et al., 2020). Also, greater adherence to this type of diet frequently correlates with higher odds of developing both early and advanced forms of AMD (Amirul Islam et al., 2014; Chiu et al., 2014; Zhang et al., 2026).

Table 1. Summary of Dietary Factors and Their Association with Age-Related Macular Degeneration.

Dietary factor	Direction of association	Main findings
Polyphenols (class)	Protective	Reduce oxidative stress, inflammation, and apoptosis affecting RPE
Resveratrol	Protective	Protects the RPE and suppresses pro-inflammatory mediators; the most promising polyphenol; potentially slowing AMD progression in combination supplements
Curcumin, quercetin, hydroxytyrosol	Protective	Consistent protection of the RPE and suppression of pro-inflammatory mediators
Carotenoids (lutein/zeaxanthin, β -carotene)	Protective but inconsistent	Lower dietary intake associated with higher AMD prevalence; supplementation consistently raises serum levels and MPOD, but effect on visual acuity and disease progression is inconsistent; limited overall benefit in AREDS2
Omega-3 PUFA (DHA, EPA)	Protective in early and intermediate AMD	Protects against early and intermediate AMD; evidence for preventing progression to advanced AMD is inconclusive
Omega-6 PUFA and a high omega-6/omega-3 ratio	Harmful	Greater risk of AMD through increased inflammation and oxidative stress
Saturated fatty acids	Inconsistent	Lower risk of early AMD with higher intake in Japanese cohorts; higher levels of palmitic and pentadecylic acid linked to increased risk in a Chinese population
Mediterranean pattern	Protective	Lower risk of advanced and neovascular AMD and slower progression; may act synergistically with AREDS2 supplementation
Western pattern	Harmful	Greater adherence correlates with higher odds of developing both early and advanced AMD
Oriental pattern	Protective	Strong inverse association with both early and advanced AMD
Breakfast and Caribbean patterns	Protective	Associated with reduced prevalence of advanced AMD
Salad pattern	No significant association	Not significantly related to the prevalence of AMD

4. CONCLUSION

Considering all the information and despite the fact that, in many cases, the results are still inconclusive, we can assume that the diet is potentially an important contributor to AMD pathogenesis. Therefore, implementing the correct type of diet and supplementation may have a protective effect on patients' vision by reducing the risk of onset or progression of AMD. Nonetheless, further studies are required for a thorough understanding of this subject.

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Authors' Contributions

Writing article manuscript – W.B., P.P., D.P., S.B., K.S., A.K., K.F., K.B.-C.; Research design – D. P., K. B.-C.; Performing the research – S. B., K. F.; Revising and editing – W. B., P. P., K. S., A. K. All authors have contributed equally to the article. All authors have read and agreed to the published version of the manuscript.

Informed consent

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Ethical approval

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interest or personal relationship that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study are present in the paper

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