

# Nutrition in Clinical Optometry

Paula R Newsome, OD, MS, FAAO, FAARM, CHC

Julie Poteet, OD, CNS, FAAO

The New York Times

Opinion

# Our Food Is Killing Too Many of Us

Improving American nutrition would make the biggest impact on our health care.

**By Dariush Mozaffarian and Dan Glickman**

Mr. Mozaffarian is dean of the Tufts Friedman School of Nutrition Science and Policy. Mr. Glickman was the secretary of agriculture from 1995 to 2001.

Aug. 26, 2019

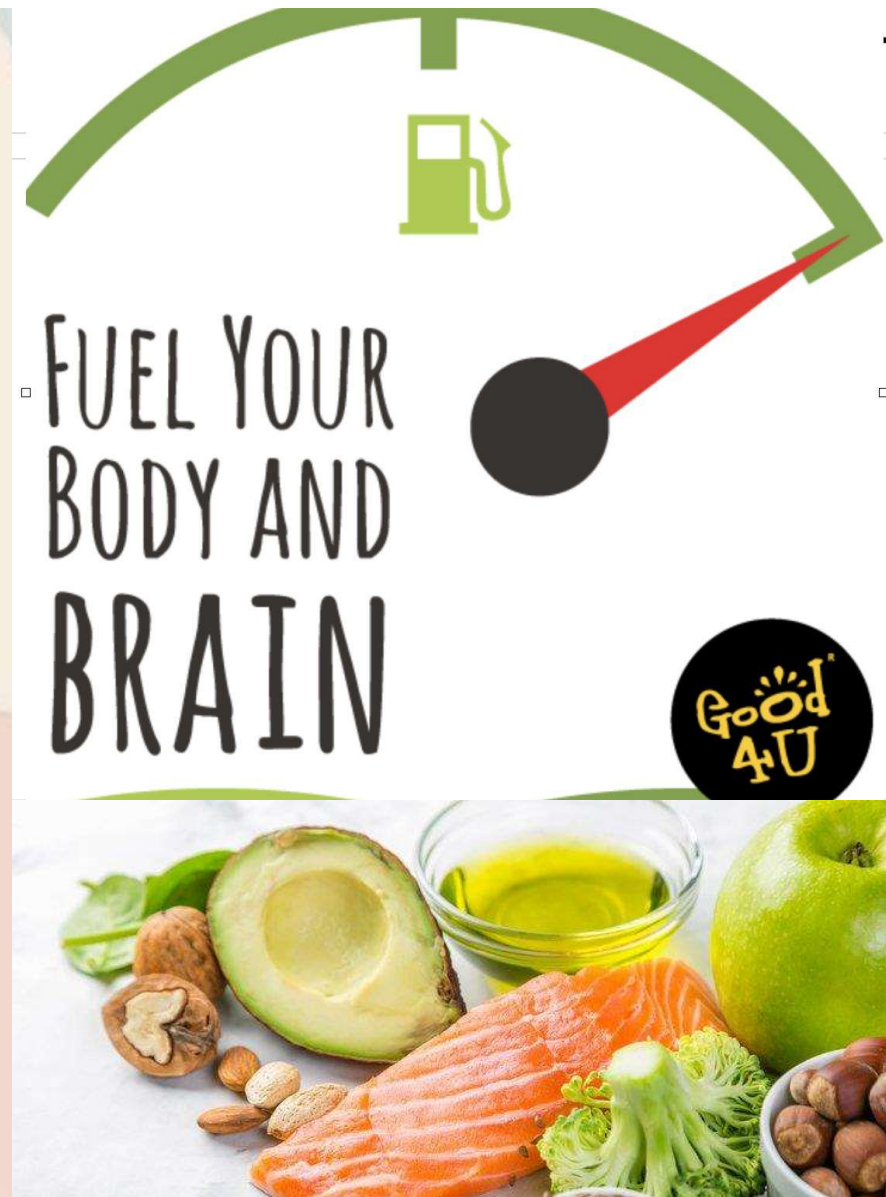


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**“Poor diet is the *leading cause* of mortality in the United States, causing more than half a million deaths per year.”**

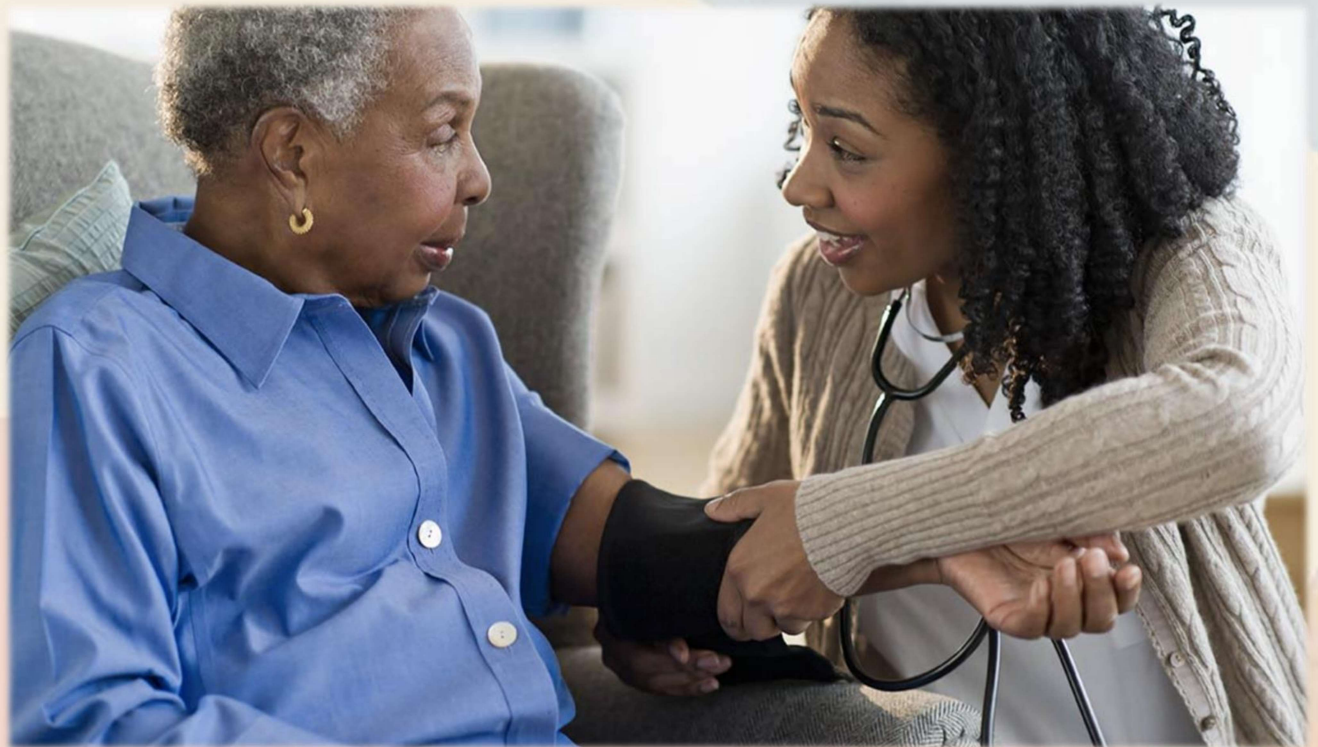
# Today's Goal

- Start thinking about food and beverage consumption differently
- Start thinking of it as fuel for the brain and the body
- Give you some tools that you can implement in your practice with your patients
- Start thinking about change behavior so that you can model what you preach

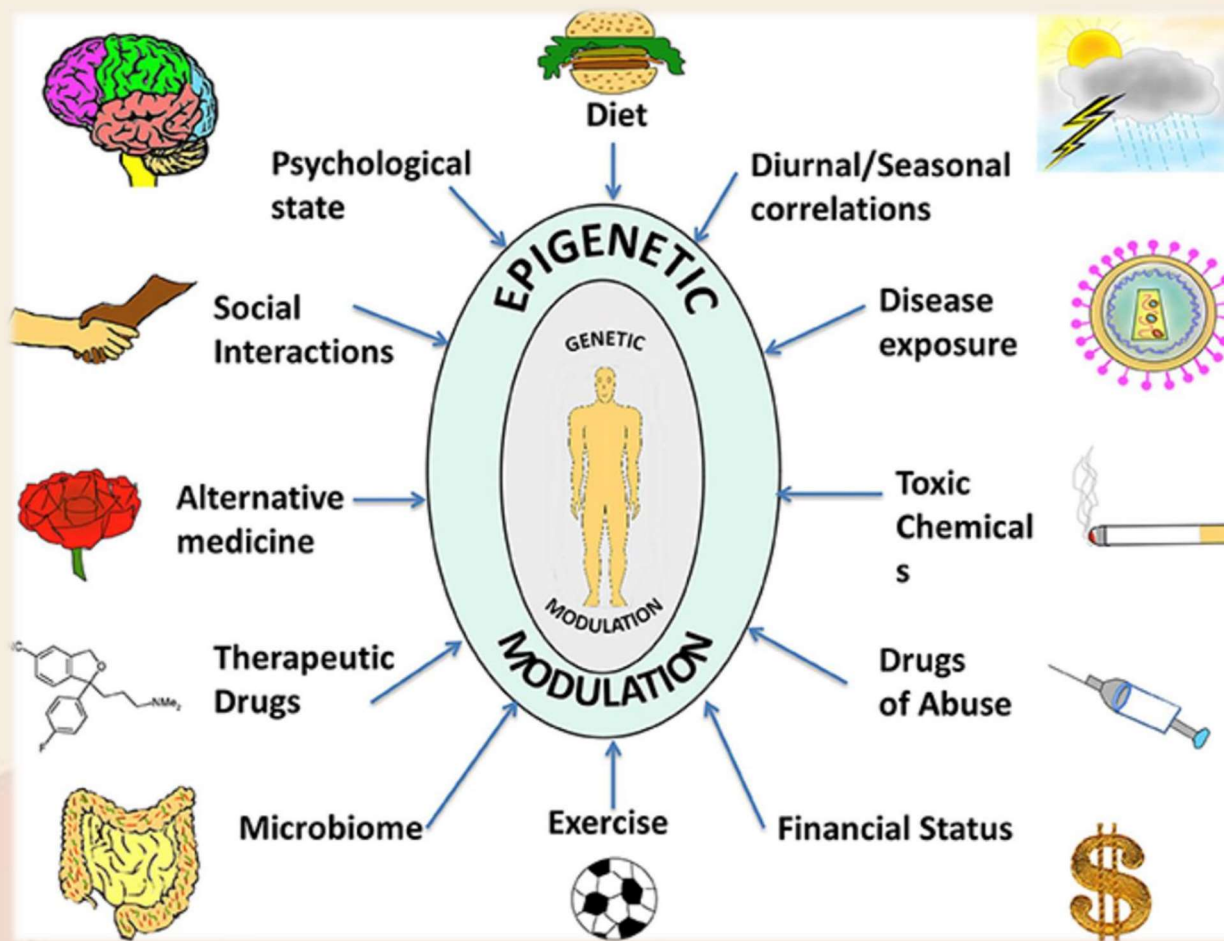


# Think About your Patients

- ▶ Patient presents with hypertension and BMI of 30+
- ▶ Also has complaints of dry eye
- ▶ What should you be thinking of and why?







**Have you ever wondered why some people got diseases and others did not?**

- ▶ It is estimated that lifestyle decisions account for over 70% of our chronic disease states
- ▶ Even when we have a genetic predisposition, we can mitigate that with healthy choices including diet, exercise and better managing stress

# Nutrition

- ▶ Nutrients are involved in all body processes at the cellular level.
- ▶ Involved for Immune system functioning
- ▶ Enables our body to repair and regenerate
- ▶ Enhances our ability to think clearly and effectively



**“Nutrition** is a process in which food is taken in and used by the body for growth, to keep the body healthy, and to replace tissue. Good **nutrition** is important for good health. Eating the right kinds of foods before, during, and after **cancer** treatment can help the patient feel better and stay stronger.” Apr 19, 2017

Nutrition in Cancer Care (PDQ®)—Patient Version - ...

National Cancer Institute (.gov) › treatment



# Nutrition

## MACRONUTRIENTS



## MICRONUTRIENTS



**Macronutrients** include protein, fat, carbohydrates and water.



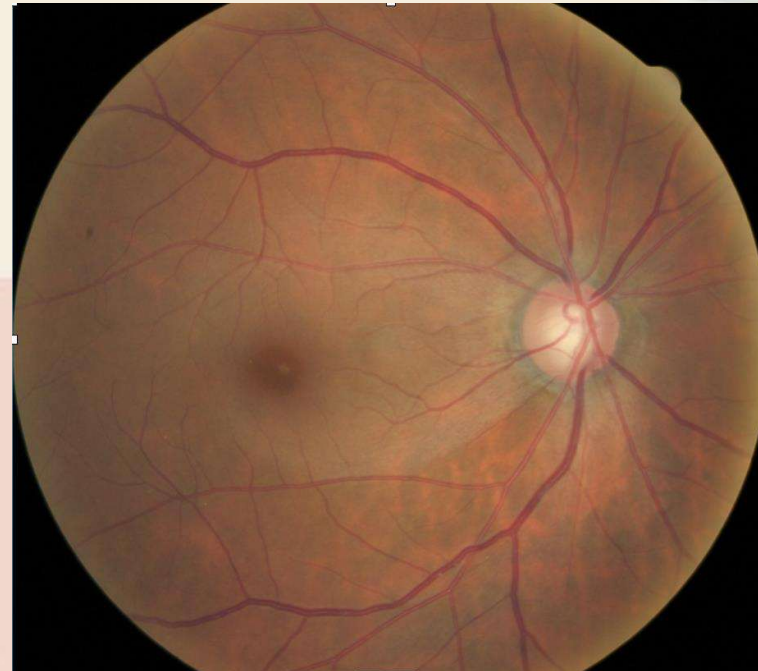
**Micronutrients** are the minerals, Vitamins and phytochemical in our food.



Deep dive into what the evidence says  
regarding the eye and nutrition



- ▶ Glaucoma
- ▶ AMD
- ▶ Diabetes



# Glaucoma

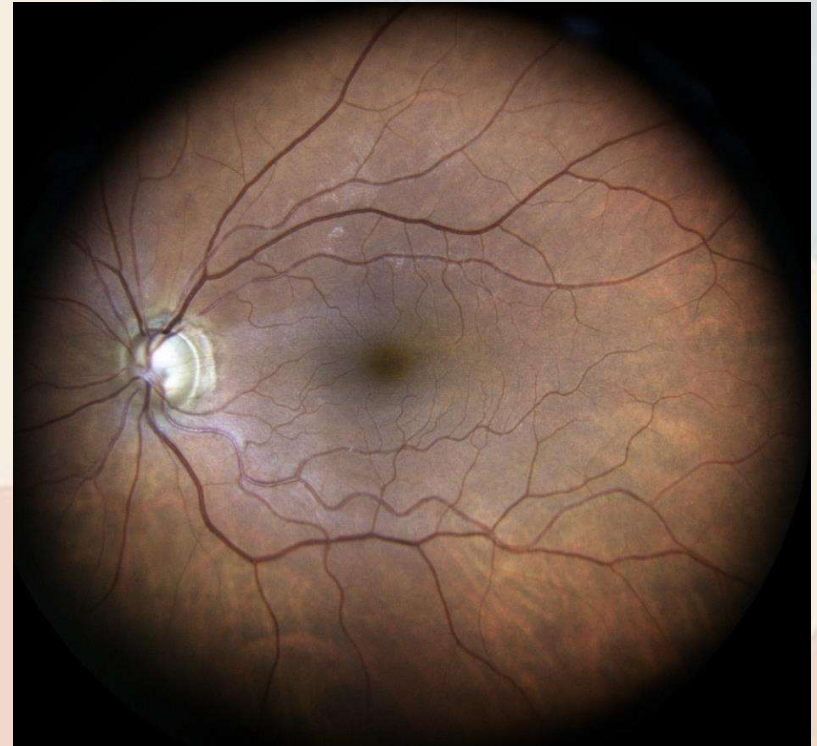
## PRIMARY OPEN-ANGLE GLAUCOMA

Glaucoma is a multifactorial optic neuropathy characterized by structural changes to the optic nerve head and peripapillary retina that are associated with characteristic functional deficits.

There is clear evidence that glaucoma is a neurodegenerative disease that affects the brain as well as the eye.

Glaucoma is associated with the following clinical features:

- Aqueous outflow restrictions
- Unphysiologic intraocular pressure
- Abnormal ocular perfusion
- Abnormal rate of apoptosis
- Progressive ganglion cell loss
- Characteristic changes in optic nerve anatomy



Punjab O, Lin S, Stamper R. Advances in mapping the glaucomatous visual field from confrontation to multifocal visual evoked potentials. The Internet Journal of Ophthalmology and Visual Science. 2006.



## Risk Factors for Glaucoma (ICD-10)

- African-American or Hispanic race
- Family history in first-degree relative
- Elevated intraocular pressure
- Abnormal optic disc appearance
- A central corneal thickness below 500 microns combined with elevated IOP

## Additional Risk Factors

- Diabetes
- Low blood pressure
- Sleeping disorders and Breathing disorders
- Trauma to the globe

# Glaucoma and Microbiome

## Oral microbiome link to neurodegeneration in glaucoma

Konstantin Astafurov<sup>1</sup>, Eman Elhawy<sup>2</sup>, Lizhen Ren<sup>1</sup>, Cecilia Q Dong<sup>2</sup>, Christina Igboin<sup>3</sup>, Leslie Hyman<sup>4</sup>, Ann Griffen<sup>3</sup>, Thomas Mittag<sup>5</sup>, John Danias<sup>6</sup>

Affiliations + expand

PMID: 25180891 PMCID: [PMC4152129](#) DOI: [10.1371/journal.pone.0104416](#)

[Free PMC article](#)

### Abstract

**Background:** Glaucoma is a progressive optic nerve degenerative disease that often leads to blindness. Local inflammatory responses are implicated in the pathology of glaucoma. Although inflammatory episodes outside the CNS, such as those due to acute systemic infections, have been linked to central neurodegeneration, they do not appear to be relevant to glaucoma. Based on clinical observations, we hypothesized that chronic subclinical peripheral inflammation contributes to neurodegeneration in glaucoma.



# Glaucoma and Microbiome

**Conclusions:** The above findings suggest that the oral microbiome contributes to glaucoma pathophysiology. A plausible mechanism by which increased bacterial loads can lead to neurodegeneration is provided by experiments in animal models of the disease and involves activation of microglia in the retina and optic nerve, mediated through TLR4 signaling and complement upregulation. The finding that commensal bacteria may play a role in the development and/or progression of glaucomatous pathology may also be relevant to other chronic neurodegenerative disorders.

# The ocular hypotensive effect of saffron extract in primary open angle glaucoma: a pilot study

▶ The progressive nature of glaucoma and its growing incidence make its therapy an important target for research. The role of oxidative damage in the pathogenesis of glaucoma makes antioxidants such as saffron extract an attractive target for potential clinical use. Herein, we evaluate the effect of aqueous saffron extract on intraocular pressure (IOP) in eyes with primary open-angle glaucoma (POAG).

## ▶ Methods

▶ Thirty-four eyes of 34 clinically stable POAG patients receiving treatment with timolol and dorzolamide eye drops were enrolled in this prospective, comparative, randomized interventional pilot study. Eligible subjects were randomized to receive 30 mg/day aqueous saffron extract orally (17 subjects, 17 eyes) or placebo (17 subjects, 17 eyes) for one month as an adjunct to timolol and dorzolamide. Following treatment, both study groups entered a one-month wash-out period. The main outcome measure was IOP during treatment and after the wash-out period.

Mean baseline IOP was  $12.9 \pm 3.7$  versus  $14.0 \pm 2.5$  mmHg in the saffron and control groups, respectively ( $p = 0.31$ ). After three weeks of treatment, IOP was significantly decreased to  $10.9 \pm 3.3$  mmHg in the saffron group as compared to  $13.5 \pm 2.3$  mmHg in the control group ( $p = 0.013$ ). At four weeks, IOP was still significantly lower in the saffron group ( $10.6 \pm 3.0$  versus  $13.8 \pm 2.2$  mmHg,  $p = 0.001$ ). At the end of the wash-out period, IOP was  $12.9 \pm 3.0$  in the saffron group versus  $14.2 \pm 2.0$  mmHg in the control group ( $p = 0.175$ ). None of the patients experienced side effects during the study and wash-out period.

## Conclusions

Oral aqueous saffron extract seems to exert an ocular hypotensive effect in primary open-angle glaucoma. This effect became evident after three weeks of therapy.

# More Studies

[J Clin Biochem Nutr.](#) 2021 Jan; 68(1): 67–72.

PMCID: PMC7844666

Published online 2020 Jul 10. doi: [10.3164/jcbn.20-50](#)

PMID: [33536714](#)

Effects of French maritime pine bark/bilberry fruit extracts on intraocular pressure for primary open-angle glaucoma

[Kaoru Manabe](#),<sup>1</sup> [Sachiko Kaidzu](#),<sup>1</sup> [Aika Tsutsui](#),<sup>1</sup> [Mihoko Mochiji](#),<sup>1</sup> [Yotaro Matsuoka](#),<sup>2</sup> [Yasutaka Takagi](#),<sup>3</sup>  
[Etsuyo Miyamoto](#),<sup>3</sup> and [Masaki Tanito](#)<sup>1,\*</sup>



> [Int J Mol Sci.](#) 2019 Aug 22;20(17):4110. doi: 10.3390/ijms20174110.

# Neuroprotective and Anti-Inflammatory Effects of a Hydrophilic Saffron Extract in a Model of Glaucoma

Jose A Fernández-Albarral <sup>1</sup>, Ana I Ramírez <sup>1 2</sup>, Rosa de Hoz <sup>1 2</sup>, Nerea López-Villarín <sup>1</sup>,  
Elena Salobar-García <sup>1</sup>, Inés López-Cuenca <sup>1</sup>, Ester Licastro <sup>1</sup>, Antonio M Inarejos-García <sup>3</sup>,  
Paula Almodóvar <sup>3</sup>, Maria D Pinazo-Durán <sup>4</sup>, José M Ramírez <sup>5 6</sup>, Juan J Salazar <sup>7 8</sup>

Affiliations + expand

PMID: 31443568 PMCID: [PMC6747458](#) DOI: [10.3390/ijms20174110](#)

**Free PMC article**



## Progress in Brain Research

Volume 256, Issue 1, 2020, Pages 79-97



# Chapter 4 - The role of commensal microflora-induced T cell responses in glaucoma neurodegeneration

Jing Tang <sup>a, c, †</sup>, Yizhen Tang <sup>b, c, †</sup>, Irvin Yi <sup>c</sup>, Dong Feng Chen <sup>c</sup> ✉

### Abstract

Over the last decade, new evidence has become increasingly more compelling that commensal microflora profoundly influences the maturation and function of resident immune cells in host physiology. The concept of gut-retina axis is actively being explored. Studies have revealed a critical role of commensal microbes linked with neuronal stress, immune responses, and neurodegeneration in the retina. Microbial dysbiosis changes the blood-retina barrier permeability and modulates T cell-mediated autoimmunity to contribute to the pathogenesis of retinal diseases, such as glaucoma. Heat shock proteins (HSPs), which are evolutionarily conserved, are thought to function both as neuroprotectant and pathogenic antigens of T cells contributing to cell protection and tissue damage, respectively. Activated microglia recruit and interact with T cells during this process.

# Latest AREDS Data

**New data from the NEI 10-year follow-up post hoc analysis of the age-related eye disease study (AREDS) and AREDS2 which was presented at ARVO's annual meeting  
May 7, 2021.**

Clinical Trial > Ophthalmology. 2021 Mar;128(3):425-442. doi: 10.1016/j.ophtha.2020.08.018.

Epub 2020 Aug 25.

# Dietary Nutrient Intake and Progression to Late Age-Related Macular Degeneration in the Age-Related Eye Disease Studies 1 and 2

Elvira Agrón <sup>1</sup>, Julie Mares <sup>2</sup>, Traci E Clemons <sup>3</sup>, Anand Swaroop <sup>4</sup>, Emily Y Chew <sup>5</sup>,  
Tiarnan D L Keenan <sup>6</sup>, AREDS and AREDS2 Research Groups

Affiliations + expand

PMID: 32858063 PMCID: PMC7902480 (available on 2022-03-01)

DOI: [10.1016/j.ophtha.2020.08.018](https://doi.org/10.1016/j.ophtha.2020.08.018)

## Abstract

**Purpose:** To analyze associations between the dietary intake of multiple nutrients and risk of progression to late age-related macular degeneration (AMD), its subtypes, and large drusen.

**Design:** Post hoc analysis of 2 controlled clinical trial cohorts: Age-Related Eye Disease Study (AREDS) and AREDS2.



## Findings:

### **Decreased Risk**

- Vitamins A, D, E, C
- B vitamins such as folate, B6, B12, thiamine, riboflavin, niacin
- Carotenoids such as alpha and beta-carotene, lutein, zeaxanthin, lycopene
- Minerals such as magnesium, calcium, zinc, iron, and copper
- Fatty acids EPA & DHA from fish or algae sources

### **Increased Risk**

- Cholesterol
- Saturated fats
- Monounsaturated fats (meat/dairy sources)
- Omega 6's
- ALA (vegetable omega 3's such as flax seeds, chia, and soy oil)
- Arachidonic acid

Research | [Open Access](#) | Published: 01 October 2014

# Monounsaturated fatty acids, olive oil and health status: a systematic review and meta-analysis of cohort studies

[Lukas Schwingshackl](#)  & [Georg Hoffmann](#)

*Lipids in Health and Disease* **13**, Article number: 154 (2014) | [Cite this article](#)

**32k** Accesses | **212** Citations | **116** Altmetric | [Metrics](#)

## Abstract

### Background

The aim of the present meta-analysis of cohort studies was to focus on monounsaturated fat (MUFA) and cardiovascular disease, cardiovascular mortality as well as all-cause mortality, and to distinguish between the different dietary sources of MUFA.

### Methods

Literature search was performed using the electronic databases PUBMED, and EMBASE until June 2nd, 2014. Study specific risk ratios and hazard ratios were pooled using a inverse variance random effect model.

**“Adopting a western diet means that MUFA is predominantly supplied by foods of animal origin, while in south European countries, extra virgin olive oil is the most dominant source of this type of fatty acid” .....**

**Results of the recently published PREDIMED trial demonstrated major cardiovascular benefits of olive oil and nuts when compared to a low-fat diet**

# What the data showed about eating a Mediterranean Type Diet

- Eating a Mediterranean diet, particularly a lot of fish, may be beneficial for those with early or even intermediate age-related macular degeneration (AMD)
- A diet high in fish can reduce the chances of developing late AMD by 65% for patients who also have protective genes
- In the general AMD population, a high fish diet reduced progression of intermediate AMD, with bilateral large drusen, to geographic atrophy by 31%.
- High adherence to a Mediterranean diet reduced progression from intermediate to late AMD, with geographic atrophy or neovascularization, by 25-to-40%.

# What the data showed about eating a Mediterranean Type Diet

**A Mediterranean diet was defined as one high in fruits, vegetables, nuts and legumes, moderate in fish, white meat and whole grains, moderate-to-low in alcohol and low in red meat and refined sugar, with a high ratio of mono-unsaturated to saturated fat intake.**





## **Dietary Nutrient Intake and Progression to Late Age-Related Macular Degeneration in the Age-Related Eye Disease Studies 1 and 2, Results continued....Summary of Interaction between Nutrient and Genotype**

- Confirmed earlier findings that the gene for complement factor H (CFH) on chromosome 1 was associated with greatly increased risk of drusen formation, while ARMS2 on chromosome 10 is associated with hemorrhage and poor visual acuity (Ophthalmology 2018;125(4):559-568).
- An earlier study by the AMD Gene Consortium found these two genes accounted for 60% of hereditary AMD risk, and these were included with another 50 previously identified AMD genetic risk markers in a genetic risk score tool (Nat Genet 2016;48:134-143).
- The AREDS/AREDS2 analysis identified additional AMD genetic risk alleles
- To find out if these associations are clinically useful, the group tested several AMD progression prediction models with and without a genetic risk score. Other factors in the models were baseline age, education, smoking status and baseline AMD severity scores in both the study and fellow eyes.
- The most powerful predictors turned out to be baseline severity scores for both the study and fellow eyes, with genetic risk scores only minimally improving performance when added to such a model. (Genetics 2017;206:119-133)

## Summary of Interaction between Nutrient and Genotype Continued...

- No interaction was observed between genetic factors and a Mediterranean diet for AMD progression
- However, for patients with a protective gene for CFH, consumption of fish was strongly associated with reduced AMD progression risk. Even low fish intake reduced risk of progression from intermediate AMD to geographic atrophy by 50%, while high fish intake reduced it 65%.
- By contrast, in those without protective alleles at CFH, no decreased risk was observed with high DHA intake. For neovascular AMD, higher DHA or EPA intake, or both, seemed to be associated with decreased risk preferentially in participants with low-risk genotypes at ARMS2, although the results were less consistent.

Clinical Trial

> Ophthalmology. 2021 Mar;128(3):425-442. doi: 10.1016/j.ophtha.2020.08.018.

Epub 2020 Aug 25.

# Dietary Nutrient Intake and Progression to Late Age-Related Macular Degeneration in the Age-Related Eye Disease Studies 1 and 2

Elvira Agrón <sup>1</sup>, Julie Mares <sup>2</sup>, Traci E Clemons <sup>3</sup>, Anand Swaroop <sup>4</sup>, Emily Y Chew <sup>5</sup>,  
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Affiliations + expand

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## Abstract

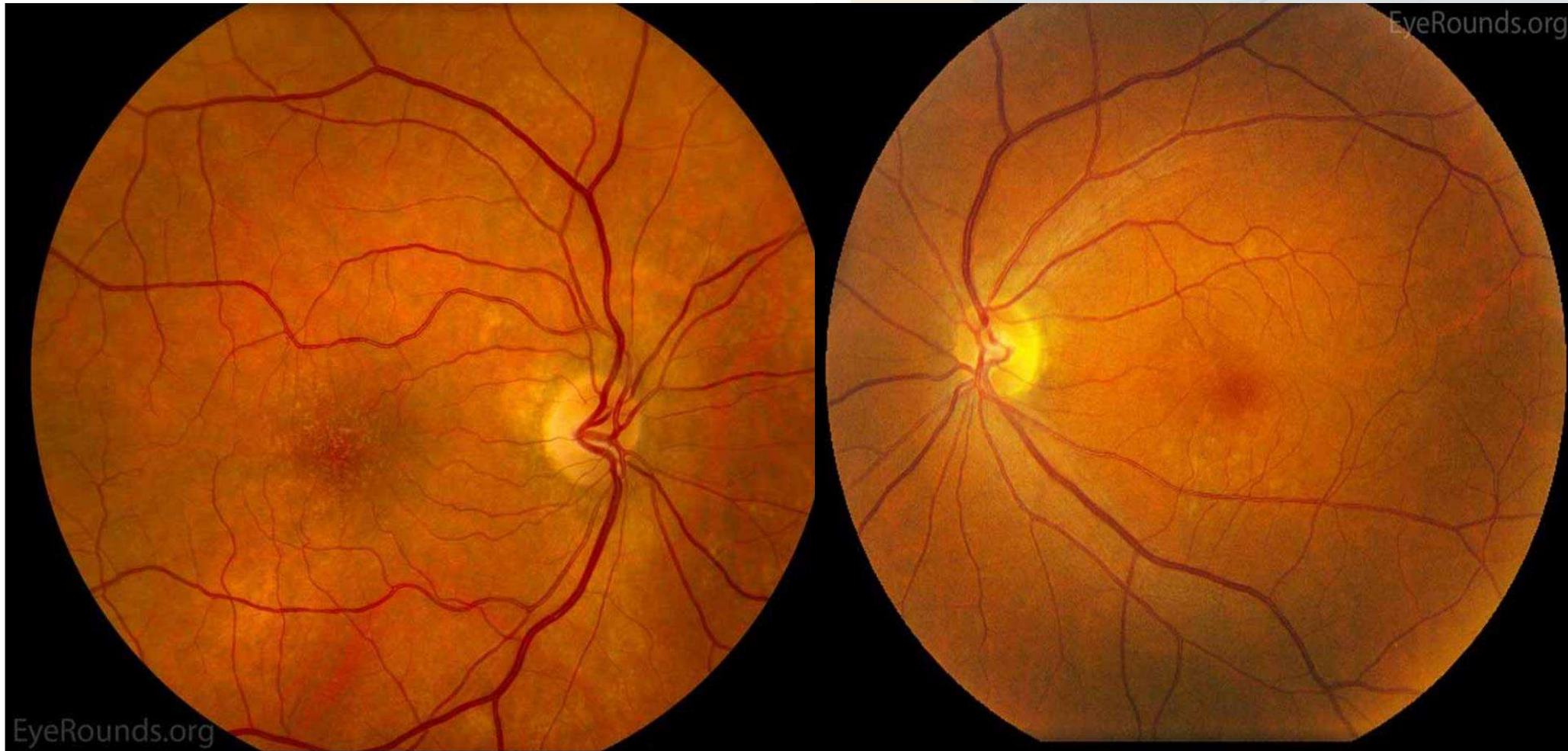
**Purpose:** To analyze associations between the dietary intake of multiple nutrients and risk of progression to late age-related macular degeneration (AMD), its subtypes, and large drusen.

**Design:** Post hoc analysis of 2 controlled clinical trial cohorts: Age-Related Eye Disease Study (AREDS) and AREDS2.

**Conclusions:** Higher dietary intake of multiple nutrients, including minerals, vitamins, and carotenoids, is associated with decreased risk of progression to late AMD. These associations are stronger for GA than for neovascular AMD. The same nutrients also tend to show protective associations against large drusen development. Strong genetic interactions exist for some nutrient-genotype combinations, particularly omega-3 fatty acids and CFH.

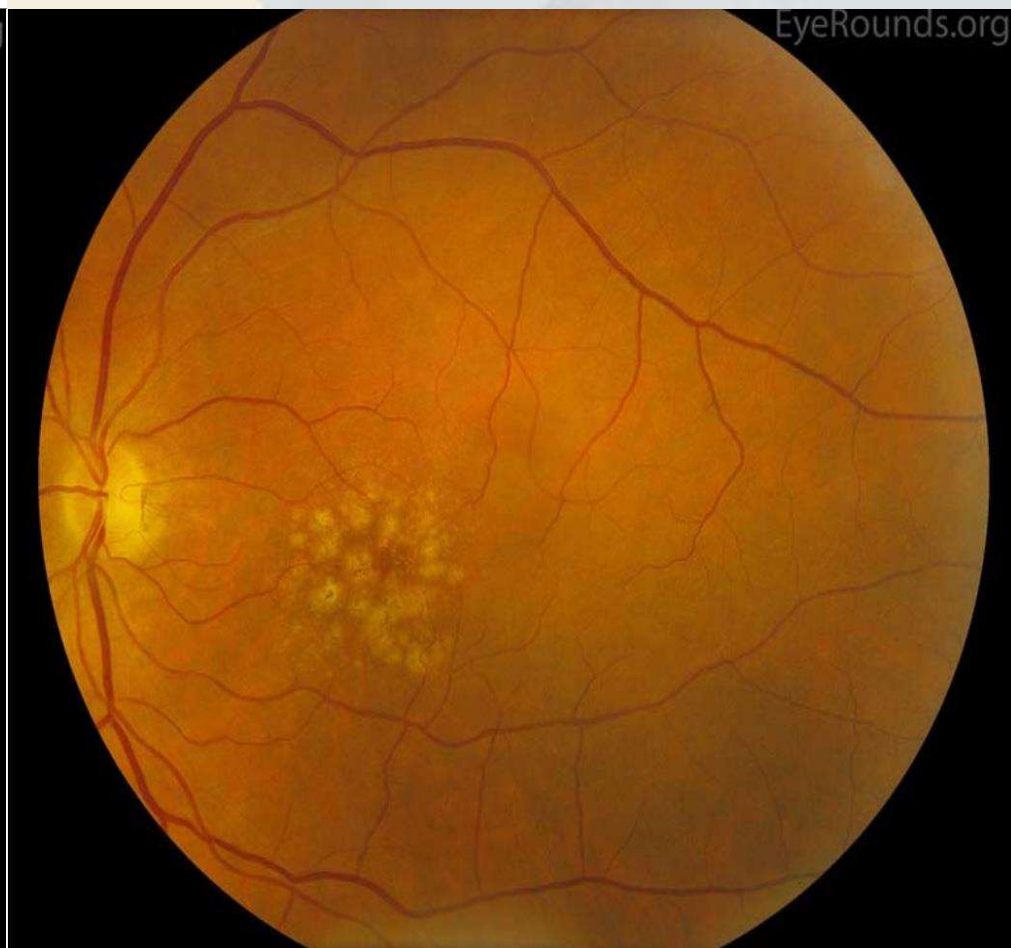
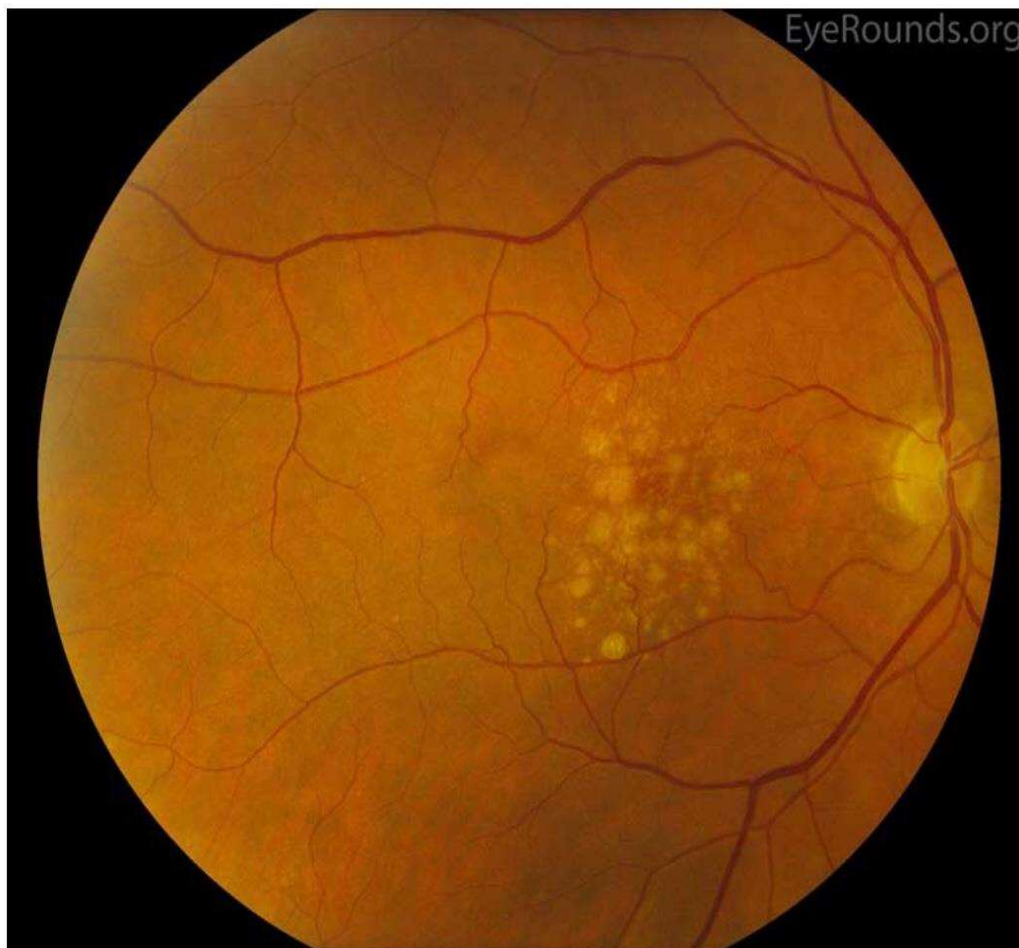


## Early AMD (AREDS Category 2)

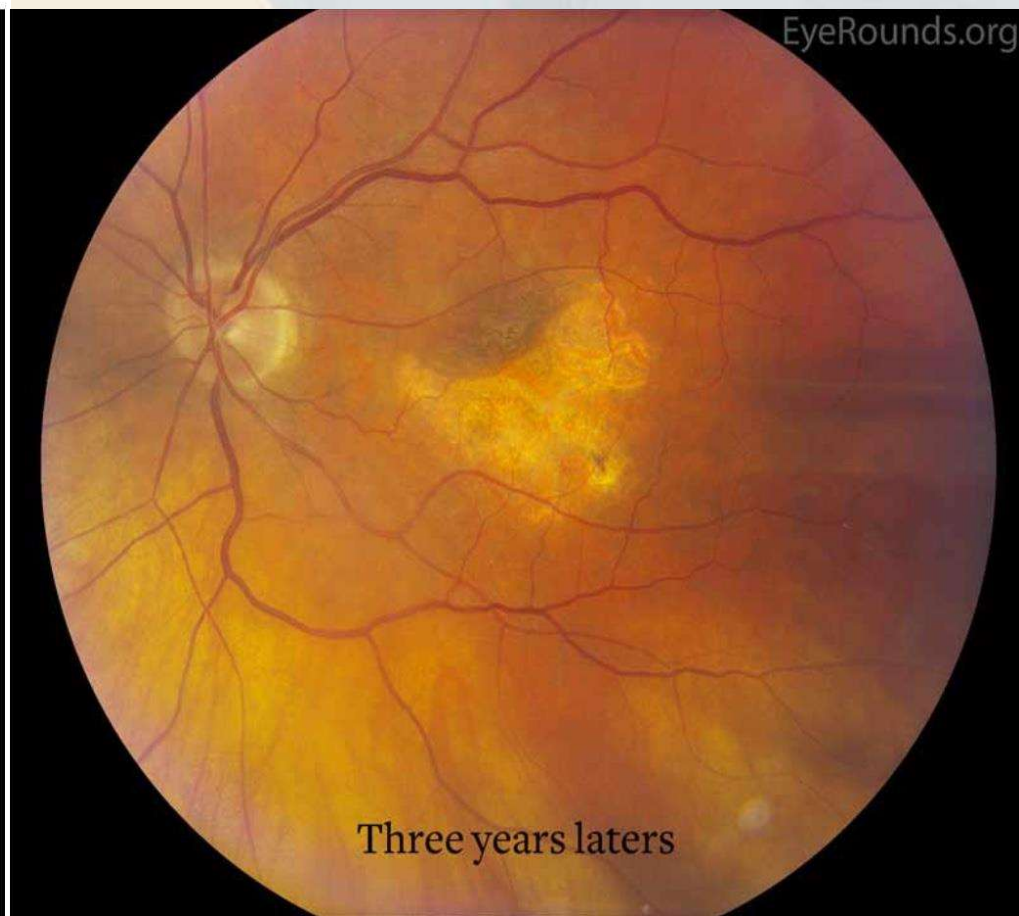
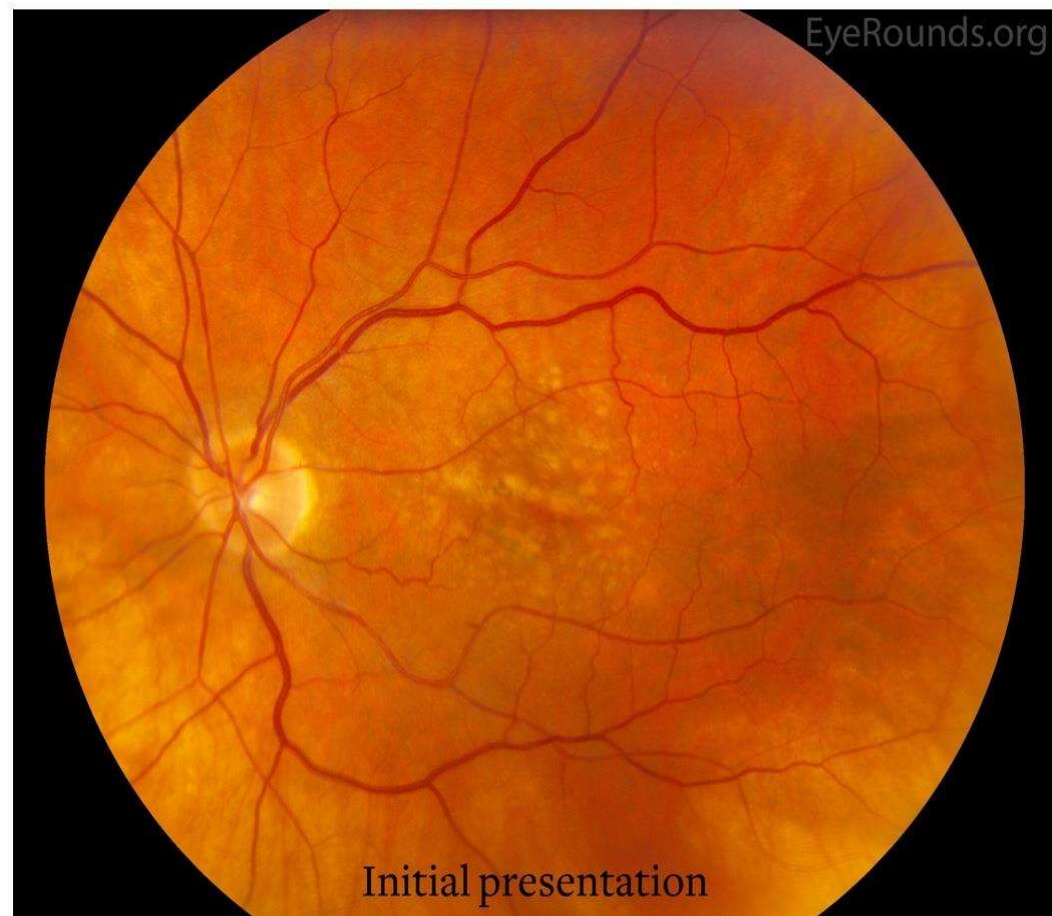




Intermediate AMD (AREDS Category 3)



Transition to Advanced Unilateral AMD (AREDS  
Category 4)





Advanced Bilateral AMD





## Systematic Review

# A Systematic Review of Carotenoids in the Management of Age-Related Macular Degeneration

Drake W. Lem <sup>1</sup>, Pinakin Gunvant Davey <sup>1,\*</sup>, Dennis L. Gierhart <sup>2</sup> and Richard B. Rosen <sup>3</sup>

<sup>1</sup> College of Optometry, Western University of Health Sciences, Pomona, CA 91766, USA; drake.lem@westernu.edu

<sup>2</sup> ZeaVision, LLC, Chesterfield, MO 63005, USA; dgierhart@zeavision.com

<sup>3</sup> Department of Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA; rosen@nyee.edu

\* Correspondence: contact@pinakin-gunvant.com; Tel.: +1-909-469-8473

**Abstract:** Age-related macular degeneration (AMD) remains a leading cause of modifiable vision loss in older adults. Chronic oxidative injury and compromised antioxidant defenses represent essential drivers in the development of retinal neurodegeneration. Overwhelming free radical species formation results in mitochondrial dysfunction, as well as cellular and metabolic imbalance, which becomes exacerbated with increasing age. Thus, the depletion of systemic antioxidant capacity further proliferates oxidative stress in AMD-affected eyes, resulting in loss of photoreceptors, neuroinflammation, and ultimately atrophy within the retinal tissue. The aim of this systematic review is to examine the neuroprotective potential of the xanthophyll carotenoids lutein, zeaxanthin, and meso-zeaxanthin on retinal neurodegeneration for the purpose of adjunctive nutraceutical strategy in the management of AMD. A comprehensive literature review was performed to retrieve 55 eligible publications, using four database searches from PubMed, Embase, Cochrane Library, and the Web of Science. Epidemiology studies indicated an enhanced risk reduction against late AMD with greater dietary consumption of carotenoids, meanwhile greater concentrations in macular pigment demonstrated significant improvements in visual function among AMD patients. Collectively, evidence strongly suggests that carotenoid vitamin therapies offer remarkable synergic protection in the neurosensory retina, with the potential to serve as adjunctive nutraceutical therapy in the management of established AMD, albeit these benefits may vary among different stages of disease.



**Citation:** Lem, D.W.; Davey, P.G.; Gierhart, D.L.; Rosen, R.B. A Systematic Review of Carotenoids in the Management of Age-Related Macular Degeneration. *Antioxidants* **2021**, *10*, 1255. <https://doi.org/10.3390/antiox10081255>

A comprehensive literature review was performed: take home message: Enough data found to suggest ALL stages of AMD benefit from supplementation



Multicenter Study > Ophthalmology. 2019 Mar;126(3):381-390.

doi: 10.1016/j.ophtha.2018.08.006. Epub 2018 Aug 13.

# Mediterranean Diet and Incidence of Advanced Age-Related Macular Degeneration: The EYE-RISK Consortium

## Abstract

**Purpose:** To investigate associations of adherence to the Mediterranean diet (MeDi) with incidence of advanced age-related macular degeneration (AMD; the symptomatic form of AMD) in 2 European population-based prospective cohorts.

**Conclusions:** Pooling data from the RS-I and Alienor Study, higher adherence to the MeDi was associated with a 41% reduced risk of incident advanced AMD. These findings support the role of a diet rich in healthful nutrient-rich foods such as fruits, vegetables, legumes, and fish in the prevention of AMD.

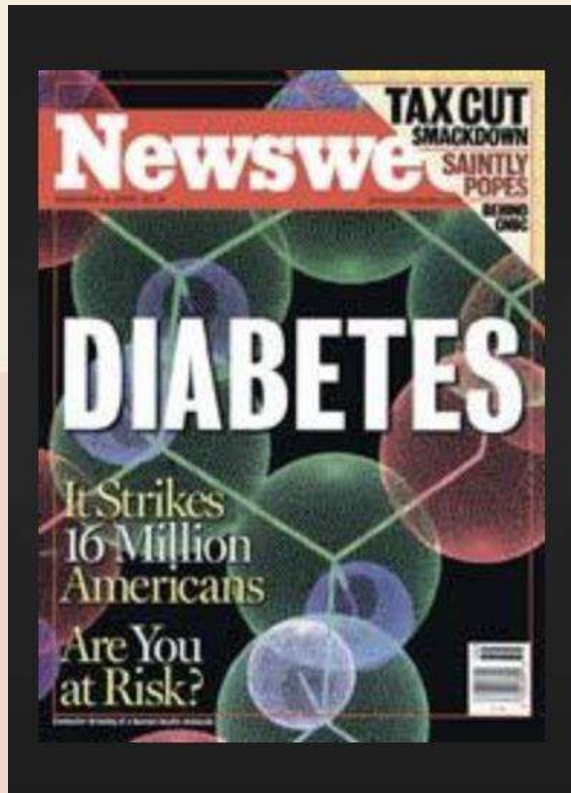
**A Mediterranean diet emphasizes eating less meat and more fish, vegetables, fruits, legumes, unrefined grains, and olive oil. Previous research has linked it to a longer lifespan and a reduced incidence of heart disease and cognitive decline.**



**“You are what you eat,” said Emily Chew, MD, a clinical spokesperson for the American Academy of Ophthalmology, who serves on an advisory board to the research group conducting the study, said in an AAO news release. “I believe this is a public health issue on the same scale as smoking. Chronic diseases such as AMD, dementia, obesity, and diabetes, all have roots in poor dietary habits. It’s time to take quitting a poor diet as seriously as quitting smoking.”**

# Diabetes

So why are we having a Diabetes epidemic?





# Diabetes

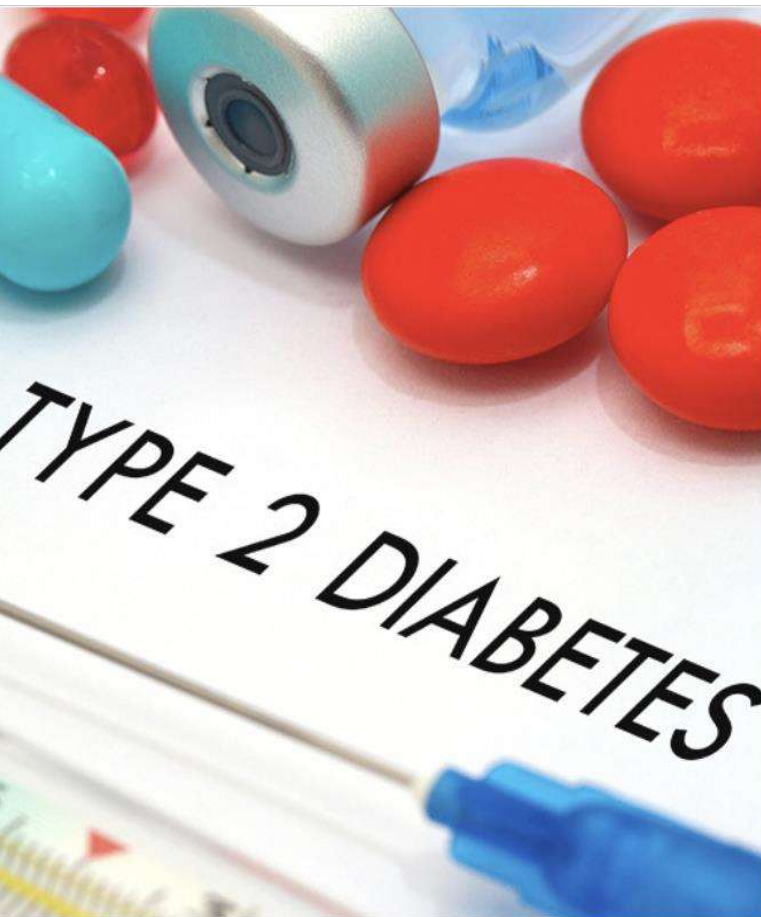


## DIABETES

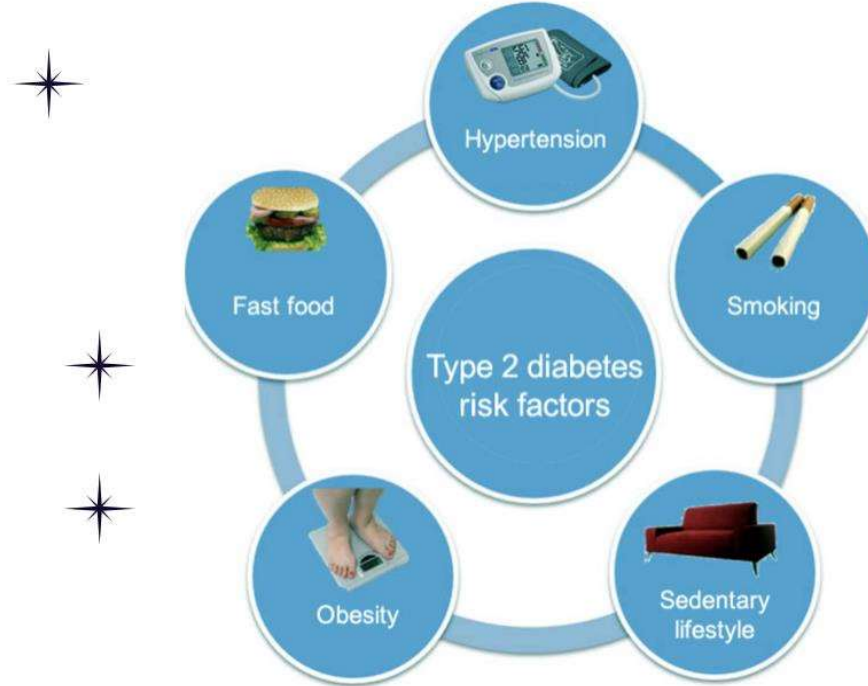
- A group of metabolic diseases defined by elevated blood glucose
- There is increased morbidity and mortality associated with this disease because of macrovascular and microvascular complications
- Long-term complications can be severe and include heart disease, kidney failure, stroke
- Diabetes profoundly impacts ocular tissue, with damage to the eye occurring even during early stages of the disease

Vieira-Potter VJ, Karamichos D, Lee DJ. Ocular Complications of Diabetes and Therapeutic Approaches. Biomed Res Int. 2016;2016:3801570. doi: 10.1155/2016/3801570. Epub 2016 Mar 28. PMID: 27119078; PMCID: PMC4826913.



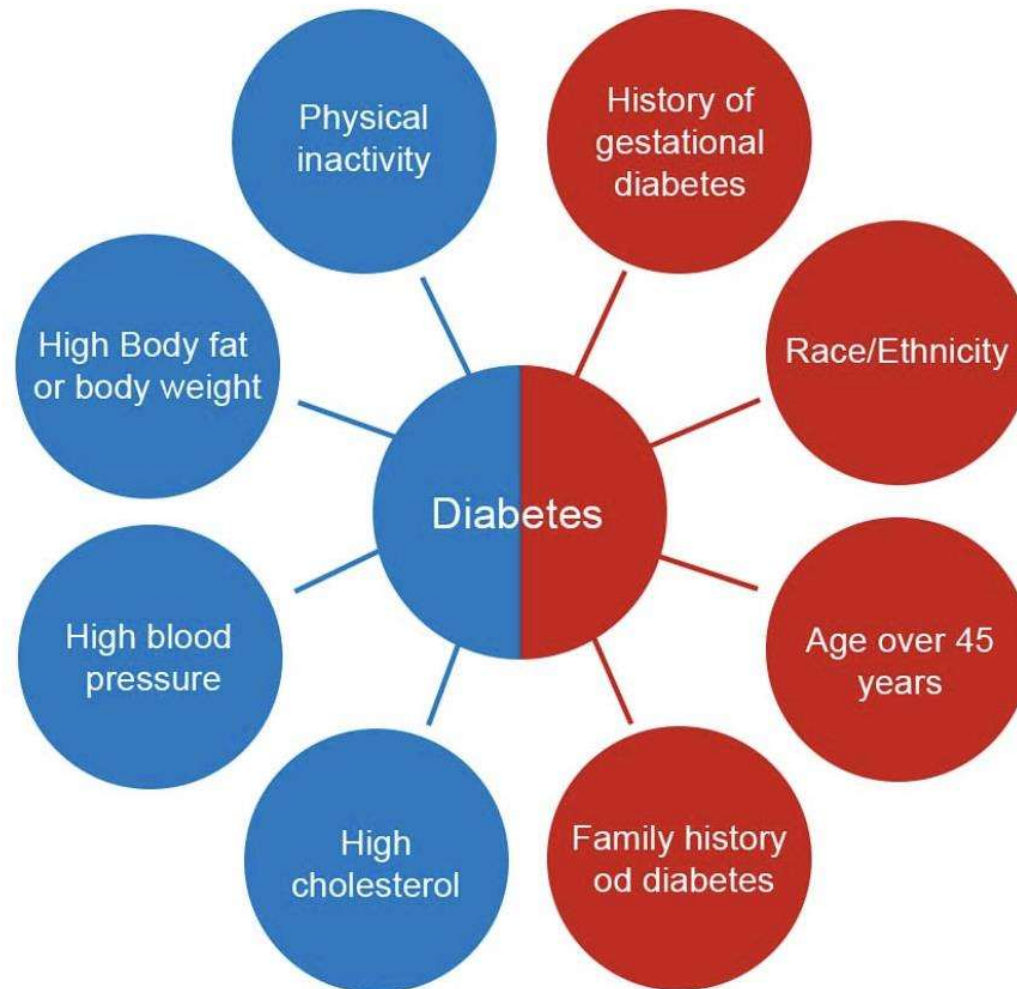


- Multifactorial condition that effects how the body handles glucose.
- About 90% of those living with Diabetes are Type 2
- In most cases can be prevented

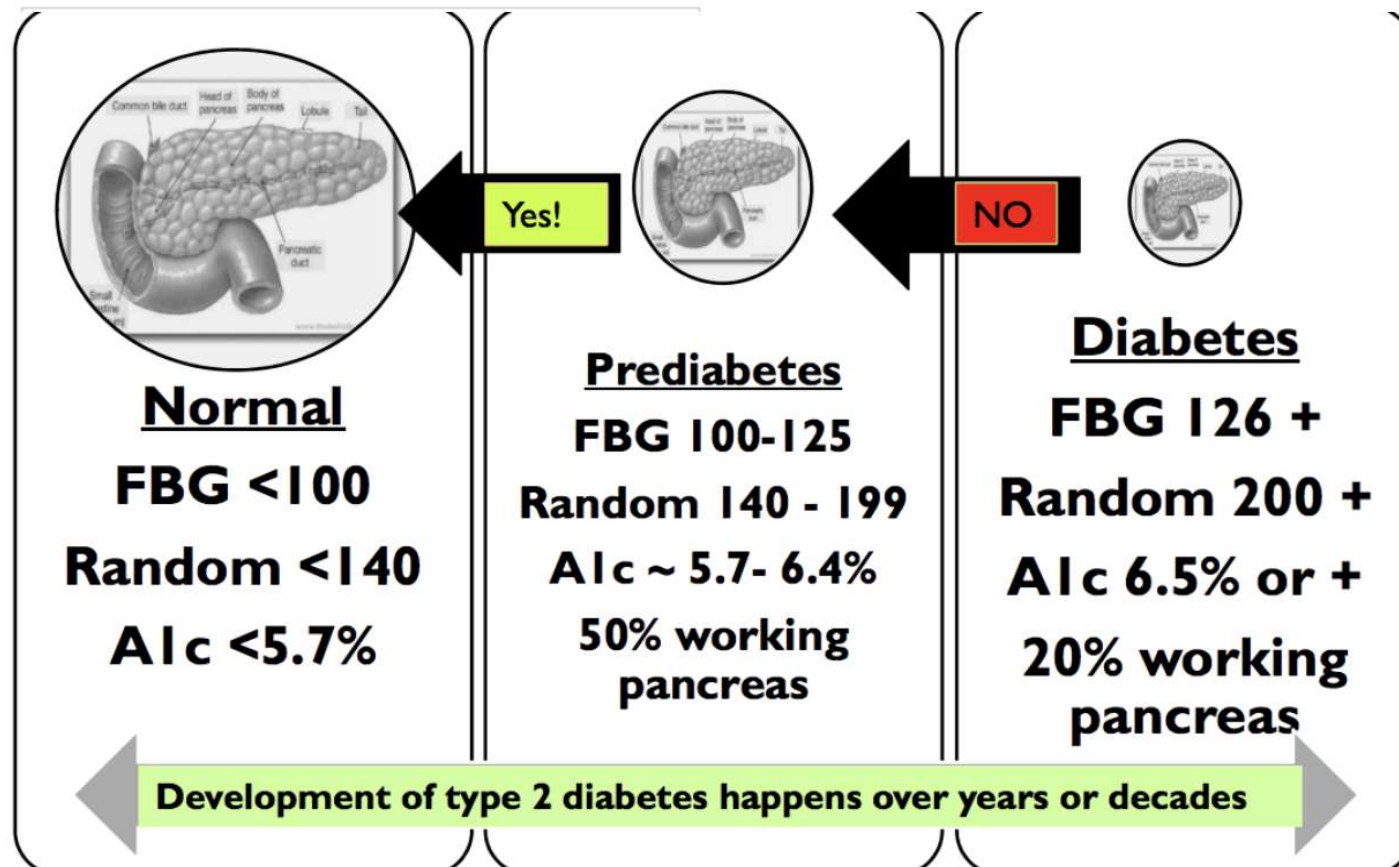


**Modifiable risk  
factors  
in diabetes**

**Non-modifiable risk  
factors  
in diabetes**



# Natural Progression of Diabetes over time



**Measuring MPOD Levels...**

**In Diabetics???.....**

**Is there a role for the supplementation  
of carotenoids in diabetic retinopathy?**





*Review*

# A Systematic Review of Carotenoids in the Management of Diabetic Retinopathy

Drake W. Lem <sup>1,†</sup> , Dennis L. Gierhart <sup>2</sup> and Pinakin Gunvant Davey <sup>1,\*,†</sup> 

**Published July 16, 2021**

**The authors performed a comprehensive literature review of the National Library of Medicine and Web of Science databases, resulting in 341 publications meeting search criteria, of which, 18 were found eligible and included in this review.**

# The Therapeutic Role of Carotenoids in Diabetic Retinopathy: A Systematic Review

This article was published in the following Dove Press journal:  
*Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*

Mohammad Fathalipour<sup>1</sup>  
Hadis Fathalipour<sup>2</sup>  
Omid Safa<sup>3</sup>  
Peyman Nowrouzi-  
Sohrabi<sup>4</sup>  
Hossein Mirkhani<sup>5</sup>  
Soheil Hassanipour<sup>6</sup>

<sup>1</sup>Department of Pharmacology and Toxicology, Faculty of Pharmacy, Hormozgan University of Medical Sciences, Bandar Abbas, Iran; <sup>2</sup>The Student Research Committee, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran; <sup>3</sup>Department of Clinical Pharmacy, Faculty of Pharmacy, Hormozgan University of Medical Sciences, Bandar Abbas, Iran; <sup>4</sup>Department of Biochemistry, Shiraz University of Medical Sciences, Shiraz, Iran; <sup>5</sup>Department of Pharmacology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran; <sup>6</sup>Gastrointestinal and Liver Diseases Research Center, Guilan University of

**Background:** Carotenoids are a large group of natural pigments that occur in many foods, fruits, and vegetables. Several studies have shown a number of biological properties of carotenoids, particularly beneficial impacts on cancer, metabolic, neurodegenerative, and cardiovascular diseases. However, recent evidence has shown that these compounds could prevent, delay, and ameliorate diabetic retinopathy (DR). The aim of current study was to review the therapeutic effects of carotenoids in the treatment of DR and discuss the molecular mechanisms that are behind these pharmacological activities.

**Methods:** Six online databases (Medline/PubMed, Scopus, Web of Knowledge, Embase, ScienceDirect, and ProQuest) were searched until September 2019. The systematic review was carried out using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

**Results:** A total of 25 studies were included after the final retrieval. A relationship was observed between carotenoids and management of DR. Findings also demonstrated that the underlying mechanism of beneficial effects of these compounds was antioxidant, anti-inflammatory, anti-angiogenic, and neuroprotective properties.

**Conclusion:** Carotenoids potentially delay the initiation and prevent the progression of DR; however, ample preclinical studies are required to confirm their effect, and adequate clinical trials are needed to really understand how well these compounds influence DR among humans.

**Keywords:** diabetic retinopathy, carotenoids, oxidative stress, inflammation, neuroprotection

# The Therapeutic Role of Carotenoids in Diabetic Retinopathy: A Systematic Review....Highlights:

- Hyperglycemia is the most important known cause of retinopathy
- Hyperglycemia-induced oxidative stress is responsible for retinal microvasculopathy
- It has also been shown that the levels of serum carotenoids are associated with the prediction and severity of DR
- Different studies have reported that carotenoids exert retinal protection during oxidative stress, which is the most important underlying mechanism involved in the pathogenesis of DR.
- Carotenoids also have improved mitochondrial dysfunction as an important source of ROS/RNS in DR.
- Treatment with carotenoids augmented the activation of retinal microglia, which have critical participation in the inflammatory responses of retina.
- Carotenoids enhanced the expression of SOD and attenuated ER stress by upregulating the expression and activation of AMP-activated protein kinase (AMPK)
- Carotenoids can significantly improve retinal endothelial dysfunction

## **The Therapeutic Role of Carotenoids in Diabetic Retinopathy: A Systematic Review....Highlights continued:**

- **Carotenoids increased the expression of retinal BDNF and prevented retinal neurodegeneration.**
- **Carotenoids diminished RGC loss, thinning of the different retinal layers including total retina (TR), inner plexiform layer (IPL), inner nuclear layer (INL), outer retinal layers (ORL), and retina photoreceptor layer (RPL) in animal models of diabetes.**

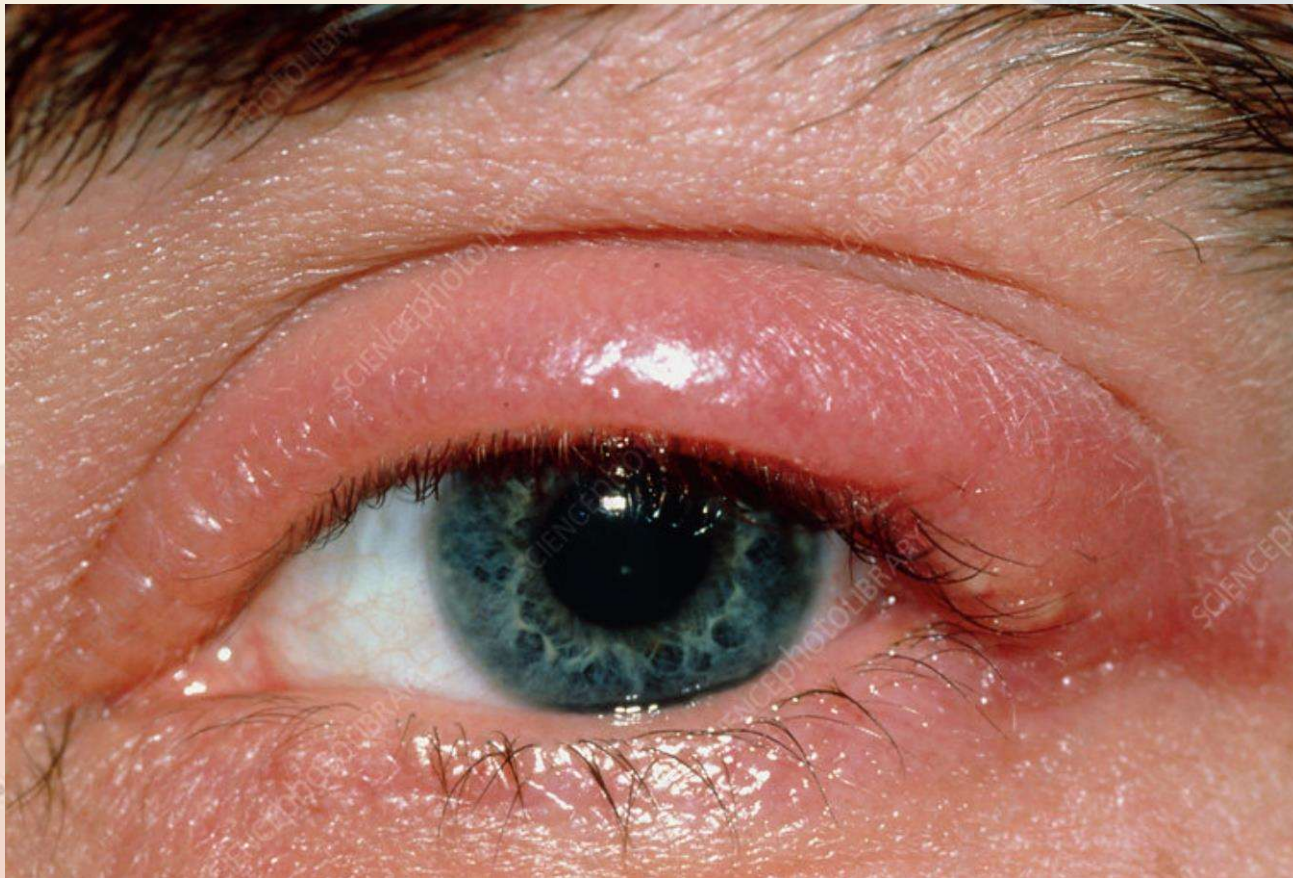
### **Conclusion:**

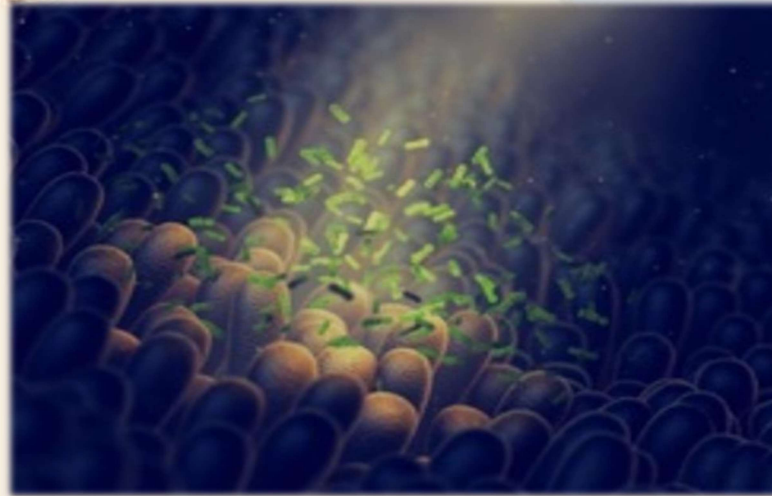
**In summary, carotenoids potentially delay the initiation and prevent the progression of DR; however, adequate clinical trials are needed to provide their effectiveness among humans.**



## Bonus information

- When prescribing Antibiotics consider prescribing probiotics.





**When prescribing antibiotics, consider concomitantly prescribing probiotics...**

Microbiome science is rapidly unfolding and what it becoming clear is that the impact our commensal microbes have on our immune system can no longer be ignored...

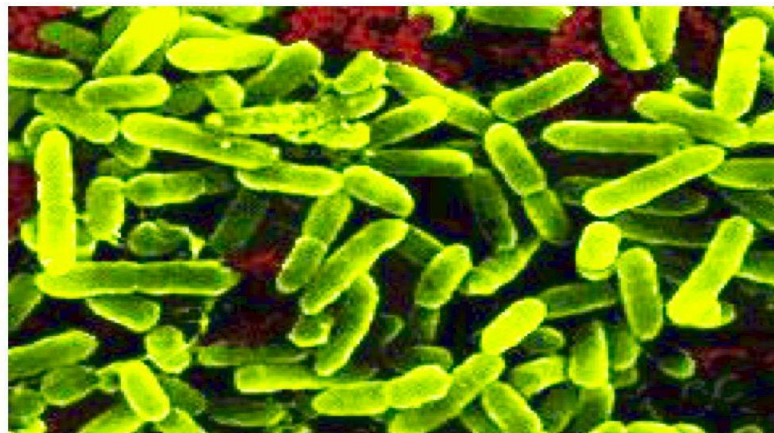
**From the 2019 Congress of Clinical Rheumatology:**

*keynote speaker James T. Rosenbaum, MD, Chief of Ophthalmology at the Legacy Devers Eye Institute in Portland and Chief of Arthritis and Rheumatic diseases at the Oregon Health and Science University spoke on the microbiome and rheumatic disease:*

**“I submit to you that in any disease that has an immune component — whether it’s Alzheimer’s, Parkinson’s, autism, atherosclerosis, obesity, diabetes and any disease that you are seeing in your clinics with an immune component — the microbiome is having some effect,” Rosenbaum told the attendees, “Whether it’s a small effect or a large effect, it is hard to say, but in these experimental rodents, it’s a huge effect. And one day, we will have therapy that is directed toward repairing or changing, or altering, that microbiome.”**

# The Human GIT Microbiota

- Can be considered an additional human organ
  - this “microbe” organ weighs 1-1.5 kg
  - rivals the liver in the number of biochemical reactions in which it participates





# The gut microbiome orchestrates human metabolism, immunity, gene expression

"The hundred trillion bacteria in the body of an adult human contain about 4 million distinct bacterial genes, **with more than 95% of them located in the large intestine.** Since most of these genes encode for enzymes and structural proteins that influence the functioning of mammalian cells, the gut microbiome can be viewed as an anaerobic bioreactor programmed to synthesize molecules which direct the mammalian immune system, modify the mammalian epigenome, and regulate host metabolism"

Galland L. Gut microbiome and brain. *J Med Food* 2014



# Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances

M. P. Francino<sup>1,2\*</sup>

**Broad-spectrum antibiotics can affect the abundances of 30% of the bacteria in the gut community, causing rapid and significant drops in taxonomic richness, diversity and evenness**

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*Edited by:*  
Peter Mullany,  
University College London, UK

*Reviewed by:*  
Polpass Arul Jose,  
Council of Scientific and Industrial  
Research – Central Salt and Marine  
Chemicals Research Institute, India  
Ashima Kushwaha Bhardwaj,  
Indian Institute of Advanced  
Research, India  
Manuela Caniça,  
National Institute of Health Doutor  
Ricardo Jorge, Portugal

*\*Correspondence:*  
M. P. Francino  
mpfrancino@gmail.com

on health, for instance through the selection of resistant opportunistic pathogens that can cause acute disease. Microbiome alterations induced by antibiotics can also indirectly affect health in the long-term. The mutualistic microbes in the human body interact with many physiological processes, and participate in the regulation of immune and metabolic homeostasis. Therefore, antibiotic exposure can alter many basic physiological equilibria, promoting long-term disease. In addition, excessive antibiotic use fosters bacterial resistance, and the overly exposed human microbiome has become a significant reservoir of resistance genes, contributing to the increasing difficulty in controlling bacterial infections. Here, the complex relationships between antibiotics and the human microbiome are reviewed, with focus on the intestinal microbiota, addressing (1) the effects of antibiotic use on the composition and function of the gut microbiota, (2) the impact of antibiotic-induced microbiota alterations on immunity, metabolism, and health, and (3) the role of the gut microbiota as a reservoir of antibiotic resistances.

**Keywords:** antibiotics, human gut microbiota, autoimmunity, immunotolerance, atopy, inflammation, dysbiosis, resistance reservoir



# Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances

M. P. Francino<sup>1,2\*</sup>

**Once antibiotic treatment has stopped, the microbiota may present a certain degree of resilience, being capable of returning to a composition similar to the original one, but the initial state is often not totally recovered.**

*Edited by:*  
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University College London, UK

*Reviewed by:*  
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Chemicals Research Institute, India  
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National Institute of Health Doutor  
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M. P. Francino  
mpfrancino@gmail.com

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# Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances

M. P. Francino<sup>1,2\*</sup>

**In fact, antibiotic-induced microbiota alterations can remain after long periods of time, spanning months and even years**

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Peter Mullany,  
University College London, UK

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Research, India  
Manuela Caniça,  
National Institute of Health Doutor  
Ricardo Jorge, Portugal

*\*Correspondence:*  
M. P. Francino  
mpfrancino@gmail.com

use, but also to their utilization in farm animals and crops. Microbiome composition can be rapidly altered by exposure to antibiotics, with potential immediate effects on health, for instance through the selection of resistant opportunistic pathogens that can cause acute disease. Microbiome alterations induced by antibiotics can also indirectly affect health in the long-term. The mutualistic microbes in the human body interact with many physiological processes, and participate in the regulation of immune and metabolic homeostasis. Therefore, antibiotic exposure can alter many basic physiological equilibria, promoting long-term disease. In addition, excessive antibiotic use fosters bacterial resistance, and the overly exposed human microbiome has become a significant reservoir of resistance genes, contributing to the increasing difficulty in controlling bacterial infections. Here, the complex relationships between antibiotics and the human microbiome are reviewed, with focus on the intestinal microbiota, addressing (1) the effects of antibiotic use on the composition and function of the gut microbiota, (2) the impact of antibiotic-induced microbiota alterations on immunity, metabolism, and health, and (3) the role of the gut microbiota as a reservoir of antibiotic resistances.

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# Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances

M. P. Francino<sup>1,2\*</sup>

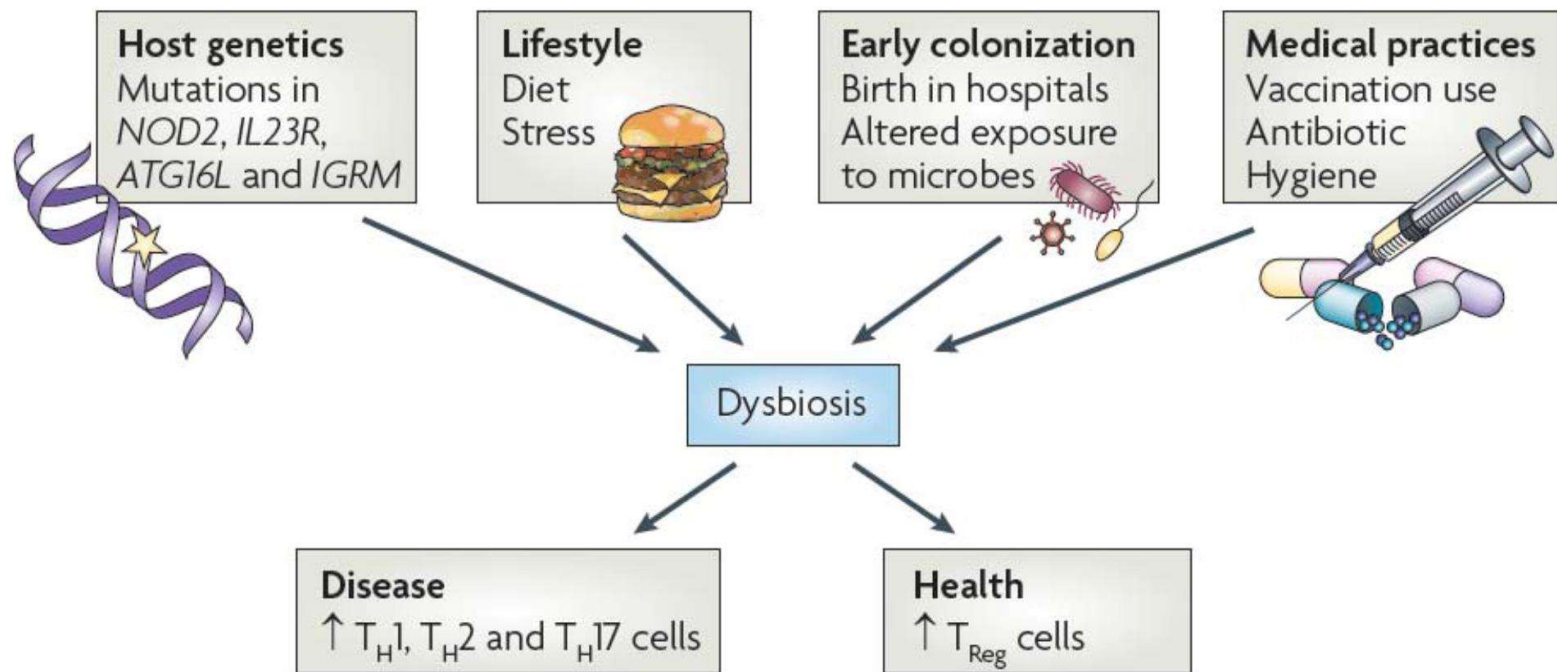
**Atopic, inflammatory and autoimmune diseases have been linked to gut microbiota dysbiosis, and, in some cases, significant associations have been established between these diseases and the intake of antibiotics during early life.**

*Edited by:*  
Peter Mullany,  
University College London, UK

*Reviewed by:*  
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“...the composition of microbiota can shape a healthy immune response or predispose to disease.”



# A practical guide for probiotics applied to the case of antibiotic-associated diarrhea in The Netherlands

[Valeria Agamennone](#), [Cyrille A. M. Krul](#), [Ger Rijkers](#) & [Remco Kort](#) 

[BMC Gastroenterology](#) **18**, Article number: 103 (2018) | [Cite this article](#)

**31k** Accesses | **16** Citations | **29** Altmetric | [Metrics](#)

## Abstract

### Background

Antibiotic-associated diarrhea (AAD) is a side-effect frequently associated with the use of broad spectrum antibiotics. Although a number of clinical studies show that co-administration of specific probiotics reduces the risk for AAD, there is still unclarity among healthcare professionals on the recommendation of probiotic products. This paper aims at a practical guide to inform healthcare professionals, patients and consumers about the exact product characteristics of available probiotics with a proven efficacy to prevent AAD.

**“We conclude that there is sufficient evidence to make a recommendation for the use of specific probiotic products for the prevention of antibiotic associated diarrhea. In particular, we provide a three-star recommendation for preparations with a minimal daily dose of  $2 \times 10^9$  CFU of the probiotic strain *Lactobacillus rhamnosus* GG.”**





## Probiotics for the prevention of antibiotic-associated diarrhea in children

**Published:**  
30 April 2019

**Authors:**  
Guo Q, Goldenberg JZ, Humphrey  
C, El Dib R, Johnston BC

### What is antibiotic-associated diarrhea?

Antibiotic-associated diarrhea (AAD) occurs when antibiotics disturb the natural balance of "good" and "bad" bacteria in the intestinal tract causing harmful bacteria to multiply beyond their normal numbers. The symptoms of AAD include frequent watery bowel movements and crampy abdominal pain.



Who is talking about this article?



**“Among the various probiotics evaluated, *Lactobacillus rhamnosus* or *Saccharomyces boulardii* at 5 to 40 billion colony forming units/day appear most appropriate for preventing AAD in children receiving antibiotics.”**



# Questions?

[drprnewsome@gmail.com](mailto:drprnewsome@gmail.com)

[drjuliepoteet@gmail.com](mailto:drjuliepoteet@gmail.com)