

# nūretin Clinical Fact Sheet

nūretin is a new approach to delay the onset and slow the progression of Diabetic Retinopathy.

Mounting Evidence that Docosahexaenoic Acid Can Delay the Onset and Slow the Progression of Diabetic Retinopathy in Patients with Diabetes

## Diabetes Diagnosis

[Serum Omega-3 Polyunsaturated Fatty Acids and Risk of Incident Type 2 Diabetes in Men: The Kuopio Ischemic Heart Disease Risk Factor Study](#)

**Published:** Diabetes Care 2014 Jan; 37(1): 189-196.

### The Abstract:

Objective: The relationship between fish or omega-3 polyunsaturated fatty acids (PUFAs) and type 2 diabetes is inconclusive. Even contaminants in fish, such as mercury, may modify the effects. We investigated the associations between serum omega-3 PUFAs eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and risk of incident type 2 diabetes in middle-aged and older Finnish men.

### Research and Design Methods:

A total of 2,212 men from the prospective, population-based Kuopio Ischemic Heart Disease Risk Factor study, aged 42–60 years and free of type 2 diabetes at baseline in 1984–1989, were investigated. Serum PUFA and hair mercury were used as biomarkers for exposure. Dietary intakes were assessed with 4-day food recording. Type 2 diabetes was assessed by self-administered questionnaires and fasting and 2-h oral glucose tolerance test blood glucose measurement at re-examination rounds 4, 11, and 20 years after the baseline and by record linkage to hospital discharge registry and reimbursement register on diabetes medication expenses. Cox proportional hazards models were used to analyze associations.

### Results:

During the average follow-up of 19.3 years, 422 men developed type 2 diabetes. Men in the highest versus the lowest serum EPA + DPA + DHA quartile had 33% lower multivariate-adjusted risk for type 2 diabetes (95% CI 13–49; P trend 0.01). No statistically significant associations were observed with serum or dietary ALA, dietary fish or EPA + DHA, or hair mercury.

### Conclusions:

Serum long-chain omega-3 PUFA concentration, an objective biomarker for fish intake, was associated with long-term lower risk of type 2 diabetes.

### Study Authors:

Jyrki K. Virtanen, Jaakko Mursu, Sari Voutilainen, Matti, Uusitupa and Tomi-Pekka Tuomainen.

## Diabetes Diagnosis

[Omega-3 Fatty Acids Protect Eyes Against Retinopathy, Study Finds](#)

**Published:** National Institutes of Health, June 24, 2007.

Omega-3 polyunsaturated fatty acids protect against the development and progression of retinopathy, a deterioration of the retina, in mice. This is the major finding of a study that appears in the July 2007 issue of the journal Nature Medicine. The study was a collaborative effort by researchers at Children's Hospital Boston, the primary pediatric teaching affiliate of Harvard Medical School, Brigham and Women's Hospital, Massachusetts General Hospital, the University of Goteborg in Sweden, and the National Eye Institute (NEI)

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and National Institute on Alcohol Abuse and Alcoholism (NIAAA) of the National Institutes of Health (NIH).

**Paul A. Sieving, M.D., Ph.D., director of the NEI, said, “This study explores the potential benefit of dietary omega-3 fatty acids in protecting against the development and progression of retinal disease. The study gives us a better understanding of the biological processes that lead to retinopathy and how to intervene to prevent or slow disease.”**

The researchers studied the effect of the omega-3 fatty acids EPA and DHA, derived from fish, and the omega-6 fatty acid arachidonic acid on the loss of blood vessels, the re-growth of healthy vessels, and the growth of destructive abnormal vessels in a mouse model of oxygen-induced retinopathy. The retinopathy in the mouse shares many characteristics with retinopathy of prematurity (ROP) in humans. ROP is a disease of the eyes of prematurely born infants in which the retinal blood vessels increase in number and branch excessively, sometimes leading to bleeding or scarring. Infants who progress to a severe form of ROP are in danger of becoming permanently blind. There are also aspects of the disease process that may apply to diabetic retinopathy, a disease in which blood vessels swell and leak fluid or grow abnormally on the surface of the retina, and age-related macular degeneration (AMD), a disease of the macula, the part of the retina responsible for central vision, and a leading cause of vision loss in Americans 60 years of age and older.

The researchers found that increasing omega-3 fatty acids and decreasing omega-6 fatty acids in the diet reduced the area of vessel loss that ultimately causes the growth of the abnormal vessels and blindness. Omega-6 fatty acid contributes to the growth of abnormal blood vessels in the retina.

“Our findings represent new evidence suggesting the possibility that omega-3 fatty acids act as protective factors in diseases that affect retinal blood vessels,” said John Paul SanGiovanni, Sc.D., NEI staff scientist and the other lead author of the study.

“This is a major conceptual advance in the effort to identify modifiable factors that may influence inflammatory processes implicated in the development of common sight-threatening retinal diseases.”

## Results:

These study results, SanGiovanni emphasized, are important because they provide a reasonable biological explanation for findings from a number of human studies on diet and retinal disease, and they identify low-cost and widely available nutrient-based treatment approaches that may show merit in future research on diseases that damage retinal blood vessels and nerve cells.

## Mild Diabetic Retinopathy

[Dietary Marine Omega-3 Fatty Acids and Incident Sight-Threatening Retinopathy in Middle-Aged and Older Individuals with Type 2 Diabetes](#)

## Published:

JAMA Ophthalmology October 2016 Volume 134, Number 10.

## The Abstract:

Diabetic Retinopathy (DR) is a devastating complication of individuals with type 2 diabetes mellitus. The retina is rich in long-chain O-3 polyunsaturated fatty acids long-chain, which are substrate for oxylipins with anti-inflammatory and antiangiogenic properties. Experimental models support dietary long-chain protection against DR, but clinical data are lacking.

## Objective:

To determine whether long-chain intake relates to a decreased incidence of sight-threatening DR in individuals with type 2 diabetes older than 55 years.

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## Design, Setting, and Participants:

In late 2015, we conceived a prospective study within the randomized clinical trial Prevención con Dieta Mediterránea (PREDIMED), testing Mediterranean diets supplemented with extra virgin olive oil or nuts vs a control diet for primary cardiovascular prevention. The trial was conducted in primary health care centers in Spain. From 2003 to 2009, 3614 individuals aged 55 to 80 years with a previous diagnosis of type 2 diabetes were recruited. Full data were available for 482 participants (48% men; mean age 67 years).

## Exposures:

Meeting the dietary long-chain recommendation of at least 500 mg/d for primary cardiovascular prevention, as assessed by a validated food-frequency questionnaire.

## Main Outcomes and Measures:

The main outcome was incident DR requiring laser photocoagulation, vitrectomy, and/or antiangiogenic therapy confirmed by an external adjudication committee.

## Results:

Of the 3482 participants, 48% were men and the mean age was 67 years. A total of 2611 participants (75%) met target long-chain recommendation. During a median follow-up of 6 years, we documented 69 new events. After adjusting for age, sex, intervention group, and lifestyle and clinical variables, participants meeting the long-chain recommendation at baseline ( $\geq 500$  mg/d) compared with those not fulfilling this recommendation ( $< 500$  mg/d) showed a 48% relatively reduced risk of incident sight-threatening DR, with a hazard ratio of 0.52 (95% CI, 0.31-0.88;  $P = .001$ ). This association was slightly stronger for yearly updated long-chain intake (relative risk, 0.48; 95% CI, 0.28-0.82;  $P = .007$ ).

## Conclusions and Relevance:

In middle-aged and older individuals with type 2 diabetes, intake of at least 500 mg/d of dietary long-chain, easily achievable with 2 weekly servings of oily fish, is associated with a decreased risk of sight-threatening DR. Our results concur with findings from experimental models and the current model of DR pathogenesis.

## Study Authors:

Aleix Sala-Vila, DPharm, PhD; Andrés Díaz-López, RD, et.al., for the Prevención con Dieta Mediterránea (PREDIMED) Investigators

## [Severe Diabetic Retinopathy/Macular Edema Combined Intravitreal Ranibizumab and Oral Supplementation with Docosahexaenoic Acid and Antioxidants for Diabetic Macular Edema](#)

## Published:

Retina. 2017 Jul;37(7):1277-1286. doi: 10.1097.

## The Abstract:

To assess the 2-year effectiveness of intravitreal ranibizumab combined with a dietary supplement rich in Docosahexaenoic Acid (DHA) plus antioxidants in 62 patients with diabetic macular edema.

## Methods:

In a randomized single-blind controlled study, 33 subjects (42 eyes) received intravitreal ranibizumab alone and 29 (34 eyes) combined with DHA (1,050 mg/day). Monthly ranibizumab (0.5 mg) was given for the first 4 months followed by on as-needed treatment.

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## Results:

At 24 months, the difference between groups in the decrease of central subfield macular thickness was significant in favor of the DHA supplementation group (95% confidence interval of the difference 7.20-97.656;  $P = 0.024$ ), although improvement in best-corrected visual acuity measured in the Early Treatment Diabetic Retinopathy Study letters did not reach statistical significance (95% confidence interval 5.4-11.2,  $P < 0.66$ ). At 24 months, gains of  $>5$  and  $>10$  letters were significantly higher in the DHA supplementation group as compared with controls when the worse and better seeing eyes were considered but other differences at 12 months and 24 months were not found.

## Conclusion:

Intravitreal ranibizumab combined with DHA supplementation reduced central subfield macular thickness after 2 years of follow-up as compared with ranibizumab alone in patients with diabetic macular edema. This anatomical improvement was accompanied by a trend for an amelioration of vision.

## Study Authors:

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