Nutrition and Age-Related Eye Diseases: The ALIENOR (Antioxydants, Lipides Essentiels, Nutrition et Maladies Oculaires) Study.

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Abstract

Background

Worldwide, degenerative eye diseases (age-related maculopathy (ARM), cataract, glaucoma) are the main causes of visual impairment and blindness, which contribute to disability in the elderly. Mainly three types of nutritional factors are investigated for their potential protection against eye ageing: antioxidants; lutein and zeaxanthin (carotenoids which accumulate specifically in the eye); omega 3 polyunsaturated fatty acids. Few epidemiological studies have been conducted in this field, particularly in Europe.

Objective

The Alienor (Antioxydants, Lipides Essentiels, Nutrition et maladies OculaiRes) Study aims at assessing the associations of eye diseases with nutritional factors, determined from plasma measurements and estimation of dietary intakes.

Design, setting and participants

Subjects were recruited in Bordeaux (France) from the ongoing population-based 3C study. In 2006–2008, 963 subjects from the 3C Study, aged 73 years or more, had an eye examination and will have follow-up eye examinations every 2 years.

Measurements

Vascular, genetic and nutritional factors were assessed at baseline (1999–2001) and follow-up examinations of the 3C Study. Eye diseases were classified according to international classifications.

Results

Nutritional status and vascular disease and risk factors were similar between participants and non participants, except for a slight difference in plasma triglycerides and HDL-cholesterol. As expected, the prevalence of eye diseases was high: early and late ARM (28.4 % and 5.6 %, respectively), open-angle glaucoma and treated ocular hypertension (4.8 % and 10.0 %, respectively), cataract extraction (45.2 %), retinopathy (8.4 %), retinal vein occlusion (1.1 %), epiretinal membrane (3.9 %), current use of artificial tears (17.3 %).

Conclusions

This study confirms the high prevalence of eye diseases in the elderly. Its main strength is the combination of nutritional, vascular and genetic information, collected over a 7 year period of time before the first eye examination. It may help design future interventional studies, which might be common with other age-related disorders, because of common nutritional factors.

Author Keywords macular degeneration ; glaucoma ; nutrition ; antioxidants ; fatty acids ; epidemiology

The eye is considerably affected by ageing. Indeed, the prevalence of visual impairment and blindness increase exponentially with age (1). Visual impairment contributes significantly to disability in the elderly (2 –3), which represents a major challenge to our ageing societies. Worldwide, the main causes of blindness and visual impairment are degenerative eye diseases, which affect the different structures of the eye: the retina (age-related maculopathy or ARM), the lens (cataract) and the optic nerve (glaucoma) (4). Their etiologies are multifactorial, involving genetic and environmental factors. Some risk factors have been identified in the last decades, such as smoking (for cataract and ARM) (5), ultraviolet light exposure (for cataract) (6), high intraocular pressure (IOP) (for glaucoma) (7). More recently, major genetic polymorphisms associated with ARM have been described (8 –9).

There is a growing interest in the role of nutritional factors in these diseases, because they are amenable to modification, by acting on food habits or by supplementation with specific nutrients. In particular, the results of the Age-Related Eye Disease Study (AREDS), showing a reduction in the incidence of late ARM with supplementation in antioxidants and zinc, have raised the hope to prevent or delay the degenerative diseases of the eye (10).

Study rationale

Mainly three types of nutritional factors are currently investigated for their potential protection against eye ageing: antioxidants, the carotenoids lutein and zeaxanthin and omega 3 polyunsaturated fatty acids (PUFA).

The retina is particularly susceptible to oxidative stress because of the high level of in-site reactive oxygen species production, due in particular to light exposure and high metabolic activity (11). Opacification of the lens is due to oxidation of the structural proteins of the lens, inducing their aggregation (12). A role for oxidative stress in glaucoma has also been suggested (13 –14). While the role of antioxidants in the protection against the development of late ARM is supported both by epidemiological studies (15) and a large interventional trial (10), results have been more conflicting with regard to cataract. Indeed, while numerous observational studies evidenced a 20% to 50 % reduction of the risk for nuclear cataract in subjects with high dietary intakes or high plasma concentrations of vitamin C and vitamin E, several large randomized clinical trials did not show any reduction in the risk of cataract with antioxidant supplementation (15). Only the REACT study showed a limited effect of supplementation with vitamin C, E and beta-carotene on cortical cataract (16). Finally, with regard to glaucoma, very few epidemiological studies are available (17 –18).

A more recent research domain regards the role of two carotenoids, lutein and zeaxanthin, for the protection of the retina and the lens. These carotenoids accumulate in the centre of the retina, named macula, where they are known as the macular pigment (19), and they are also the only carotenoids found in the lens (20). Besides their antioxidant properties, they probably act as a filter against the phototoxic effects of blue light (19). Epidemiological data are still very scarce in this field, with few studies being prospective, and few including plasma measurements (19).

Finally, omega 3 PUFA include a precursor (alpha-linolenic acid), and three long-chain derivatives (eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA)). Long chain omega 3 PUFA have important structural and protective functions in the retina (21). A recent meta-analysis of nine epidemiological studies showed a 38 % reduced risk for ARM in subjects with high consumption of omega 3 PUFA and fish (the major dietary source of long-chain omega 3 PUFA) (22). Overall, few of these studies were prospective and none included biological measurement of fatty acids status.

Besides a potential direct effect of these nutrients in the eye, their role could be mediated by an effect on atherosclerosis and vascular diseases. Indeed, a role for antioxidants and omega 3 PUFA has been reported in vascular diseases (23 –24) and ARM and cardiovascular disease share common risk factors, such as smoking, obesity (25) and hypertension (26), suggesting a contribution of vascular disease to the pathogenesis of ARM.

Thus, there is a growing scientific background to the role of nutrition in the pathogenesis of age-related eye diseases, which may lead to prevention means for these diseases. There is a need for epidemiological prospective studies in different countries and cultures, which will take into account genetic, vascular and nutritional factors (including assessment of dietary intake and biological measurements), since all those dimensions may act in interaction. In particular, very few studies have been performed in Europe, although dietary habits and lifestyle are very different from the United States. We report the design and baseline characteristics of a population-based epidemiological study conducted in France, including the prevalence of eye diseases.

Population and methods

Study aims

The Alienor (Antioxydants, Lipides Essentiels, Nutrition et maladies OculaiRes) Study is a population-based prospective study aiming at assessing the associations of age-related eye diseases (ARM, glaucoma, cataract, dry eye syndrome) with nutritional factors (in particular antioxidants, macular pigment and fatty acids), determined from plasma measurements and estimation of dietary intakes. It also takes into account other major determinants of eye diseases, including gene polymorphisms, environmental factors and vascular factors.

A secondary aim is to assess the quality of eye care in an elderly French population, and the consequences of eye diseases and visual impairment, in particular in terms of disability and depression.

Study sample

Subjects of the Alienor Study were recruited from an ongoing population-based study on the vascular risk factors for dementia, the Three City (3C) Study (27). The 3C Study included 9294 subjects aged 65 years or more from three French Cities (Bordeaux, Dijon and

Montpellier), among which 2104 were recruited in Bordeaux. Subjects were contacted individually from the electoral rolls. They were initially recruited in 1999–2001 and followed-up about every two years since (Figure 1). Data collected at each examination included cognitive testing with diagnosis of dementia and assessment of vascular risk factors. In addition, at baseline, fasting blood and DNA samples were collected and kept frozen at − 80°C.

The Alienor study consisted in an eye examination, which was proposed to all participants in the third follow-up (2006–2007) of the 3C cohort of Bordeaux. Among the 1450 participants of the third follow-up of the Bordeaux cohort of the 3C Study, 963 (66.4 %) participated in the Alienor Study (Figure 1). A first follow-up eye examination of these subjects is currently underway and we plan to perform at least two additional follow-up examinations, about every two years.

This research followed the tenets of the Declaration of Helsinki. Participants gave written consent for the participation in the study. The design of this study has been approved by the Ethical Committee of Bordeaux (Comité de Protection des Personnes Sud-Ouest et Outre-Mer III) in May 2006.

Eye examination

The eye examination took place in the Department of Ophthalmology of the University Hospital of Bordeaux. The eye examination included a recording of ophthalmological history, measures of visual acuity and refraction, two 45° non mydriatic color retinal photographs (one centred on the macula, the other centred on the optic disc), measures of intraocular pressure and central corneal thickness and break-up time test. A self-completed questionnaire on risk factors specific to the eye (sunlight exposure, television and computer use) and dry eye symptoms (Ocular Surface Disease Index (OSDI) (28)) was filled at home and brought back on the day of the eye examination.

Visual acuity measurements included current and best corrected far visual acuity, using ETDRS charts (Light House Low Vision, New York, NY) and current and best corrected near visual acuity, using the Parinaud charts (Luneau SAS, Chartres, France), which is the usual near vision test used by French ophthalmologists. Refraction was measured using autorefractometer (Speedy K, Luneau, France). Retinal photographs were performed using a non mydriatic retinograph (TRC NW6S, Topcon, Japan). Intraocular pressure was measured with pneumotonometer (KT 800, Kowa, Japan) and central corneal thickness using Pachpen (Accutome Inc., Malvern Pa, USA). Tear break-up time (BUT) test was performed at slit lamp. A fluorescein strip (Fluo Plus, Gecis, France) was applied in the lower eyelid fornix, and the patient asked to blink three times and look straightforward. The breakup time of the tear film observed under cobalt blue filtered light of the slit lamp microscope was recorded with a stopwatch. The mean of three consecutive tear BUT tests was taken into consideration.

Retinal photographs were interpreted in duplicate by two specially trained technicians. Inconsistencies between the two interpretations were adjudicated by a retina specialist for classification of ARM and other retinal diseases, by a glaucoma specialist for classification of glaucoma. All cases of late ARM, other retinal diseases and glaucoma were reviewed and confirmed by specialists.

Classification of ARM

Retinal photographs were interpreted according to the international classification (29) and to a modification of the grading scheme used in the Multi-Ethnic Study of Atherosclerosis for drusen size, location and area (30). Late ARM was defined by the presence of neovascular ARM or geographic atrophy within the grid (3000 μm from the foveola). Neovascular ARM included serous or hemorrhagic detachment of the retinal pigment epithelium (RPE) or sensory retina, subretinal or sub-RPE hemorrhages and fibrous scar tissue. Geographic atrophy was defined as a discrete area of retinal depigmentation, 175 μm in diameter or larger, characterized by a sharp border and the presence of visible choroidal vessels. Five cases of late ARM had no gradable photographs and were classified by using ophthalmological history of ARM and ARM therapy (in particular antiangiogenic agents and photodynamic therapy), and confirmed by their treating ophthalmologist. Because etiologies of neovascular and atrophic ARM may be different, we separated two groups: subjects with neovascular ARM (with or without geographic atrophy) and subjects with late atrophic ARM (geographic atrophy without neovascular ARM).

Early ARM was classified in two groups (in the absence of late ARM): early ARM 1 (soft distinct drusen without pigmentary abnormalities or pigmentary abnormalities without large drusen (>125 μm)); early ARM 2 (soft indistinct drusen and/or reticular drusen and/or soft distinct drusen associated with pigmentary abnormalities (hyper- or hypopigmentation)). Soft distinct and indistinct drusen were larger than 125 μm in diameter and with uniform density and sharp edges or decreasing density from the center outwards and fuzzy edges, respectively. Pigmentary abnormalities were defined as areas of hyperpigmentation and/or hypopigmentation (without visibility of choroidal vessels).

Subjects were classified according to their worse eye, into one of the five exclusive groups: no ARM, early ARM 1, early ARM 2, late atrophic ARM, late neovascular ARM. These definitions of ARM are similar to those used in other large epidemiological studies of ARM, such as the Blue Mountains Eye Study (31), the Rotterdam Study (32), or the EUREYE Study (33), in order to facilitate comparisons with these studies.

Other retinal diseases

Retinopathy was defined by the presence of microaneurysms and/or soft exudates and/or blot haemorrhages and/or flame-shaped haemorrhages, anywhere on the colour photograph centred on the macula. Epiretinal membranes were defined by the presence of preretinal fibrosis, with retinal folds. The earlier stages, often named cellophane macular reflex, without retinal folds, were not recorded.

Classification of glaucoma

Glaucoma was classified according to the classification proposed by Foster PJ and colleagues (34), using two steps. Firstly, vertical cup:disc ratio (VCDR) and minimal rim:disc ratio were estimated from optic disc photographs. Subjects were classified as suspects for glaucoma when, in at least one eye, we observed a vertical cup:disc ratio greater or equal to 0.65 and/or a minimal rim:disc ratio lower or equal to 0.1 or an asymmetry of cup disc:ratio between eyes greater or equal to 0.2.

An additional eye examination was performed in 76 of 86 subjects suspect for glaucoma (88 %). This examination included a white-on-white visual field examination (Octopus 101, Interzeag International, Switzerland), an examination of the optic disc using Heidelberg Retinal Tomograph (HRT II, Heidelberg Engineering, Germany), an evaluation of the irido-corneal angle by gonioscopy, a measure of intraocular pressure using Ocular Response Analyser (Reichert Inc, New York). With regard to visual field testing, reliability was considered as acceptable when the percentages of false-positive and false-negative were below 33 %.

Glaucoma was defined according to 3 levels of evidence. In category 1, diagnosis was based on structural evidence (VCDR on optic nerve photographs greater or equal to 0.7 and/or asymmetry of VCDR greater than 0.2 and/or minimal rim:disc ratio lower or equal to 0.1) associated with functional evidence (visual field showing at least three contiguous non-edge points with corrected $p<1$ %, of which at least one point with corrected $p<0.5$ %), in the absence of other disease (in particular vascular) that might explain the findings. Category 2 was based on advanced structural damage (VCDR greater or equal to 0.8 or asymmetry of VCDR greater than 0.3) with unproven field loss (unfeasible or unreliable visual field examination). Category 3 included subjects with very low vision (visual acuity <3/60) for whom optic disc photographs and visual field could not be obtained, but glaucoma morbidity was confirmed by their treating ophthalmologist. All glaucoma cases were classified according to category 1 criteria, except one case with category 2 criteria, and one case with category 3 criteria.

Other end-points

Since the eye examination did not include pupil dilation, it was impossible to assess lens opacities. The cataract endpoints therefore relied solely on cataract extraction (confirmed by observation at slit lamp of the absence of the natural lens). Several features of dry eye syndrome were explored: self-reported dry eye, current use of artificial tears, OSDI score (28) and tear BUT test.

Nutritional data

Nutritional data have been collected during the 4 examinations performed in the framework of the 3C Study, in Bordeaux. They consist in biological measurements from the fasting blood samples performed during the baseline examination (1999–2001) and dietary assessment at baseline and follow-up examinations. Plasma vitamins A and E, malondialdehyde (MDA) and fatty acids were measured at the Laboratory of Biochemistry and Molecular Biology of the University of Bordeaux 2. Vitamin A and E were measured by reversed-phase high performance liquid chromatography (HPLC). MDA was analysed by a modified method (35). Plasma fatty acid composition was determined by gas chromatography, after extraction of plasma total lipids with hexane/isopropanol (36). In addition, measurements of plasma carotenoids are currently being performed.

With regard to dietary data, a brief dietary questionnaire was collected at baseline (1999–2001). At Bordeaux, during the first follow-up examination (2001–2002), 1796 subjects participated in a nutritional survey. A 24 h dietary recall and a food-frequency questionnaire were administered at home by dieticians. The dieticians received collective training and monitoring in order to optimize the standardization of the nutritional interviews. With regard to the 24 h dietary recall, nutrient intakes were estimated from food intakes using the BILNUT software (SCDA Nutrisoft, Cerelles, France), which includes food composition tables for France (37). When necessary, this table was completed by other sources (a French food composition table from the Institut National de la Santé et de la Recherche Médicale (38), a food composition table edited by Souci et al (39), the United States Department of Agriculture Nutrient Database, direct contact with food manufacturers and specific nutrient measurements performed by the Institut des Corps Gras (ITERG, Bordeaux, France)). Besides, the food frequency questionnaire (FFQ) included 148 food and beverage items, for which the frequency of intake was recorded in

11 classes (from never to 7 times per week), for each of the 3 main meals and 3 between-meal snacks. Concordance between FFQ and 24 h dietary recall was assessed for fatty acids, and showed acceptable correlations between number of weekly servings of foods obtained from the FFQ and the corresponding intakes of fatty acids in the dietary recall (40).

At the next two follow-ups (2003–2004 and 2006–2007) a simplified food frequency questionnaire was administered by the psychologists during the home visit, in order to detect modifications in dietary habits. We previously published detailed methods and distributions of dietary intake (41 –43) and of plasma antioxidants (44) and fatty acids (36 , 45) in the 3C Study.

Vascular factors and other variables

At each examination (baseline and follow-ups), a face-to-face administered questionnaire assessed socio-demographic data, health status and general risk factors. In particular, it included a recording of history of cardiovascular disease and vascular risk factors. For subjects who reported the occurrence of vascular events during follow-up, further medical data was obtained general practitioners, specialists and hospital records.

Examination also included an inventory of all medications used during the preceding month, which were subsequently coded according to the French translation of the WHO ATC classification (www.theriaque.org , Centre National Hospitalier d'Information sur le Médicament). The clinical examination included several measures of systolic and diastolic blood pressure, using a digital electronic tensiometer (OMRON M4) and anthropometric measurements (height, weight, and waist, arm, calf and cranial circumferences). In addition, at baseline, an ultrasound examination of the carotid arteries was performed in 73 % of participants below the age of 85 years.

Measurement of blood glucose and lipids were centralized and performed at the Biochemistry Laboratory of the University Hospital of Dijon. Centralized facilities for genotyping are provided by the Lille Genopôle. The polymorphisms of apolipoprotein E and the Y402H polymorphism of Complement Factor H are currently available on the whole cohort. Finally, a genomewide scan was performed on the whole sample (46).

Results

As expected, by comparison with non participants, participants in the Alienor Study showed some differences in socio-demographic status: they were younger (79.8 years versus 82.9 years), more often males (38.1 % in participants versus 31.4 % in non participants), had higher educational level (20.7 % with University level versus 12.5 %) and monthly income (35.6 % with income greater or equal to 2300 euros versus 27.0 %). However, after adjustment for age and gender, nutritional status was not significantly different between participants and non participants (Table 1). With regard to vascular diseases and risk factors, participants differed from non participants only for plasma triglycerides (somewhat lower) and HDL-cholesterol (slightly higher).

Table 2 shows the prevalence of major eye diseases in the participants of the Alienor study. Retinal photographs were gradable for ARM in at least one eye for 879 of 963 participants (91 %). The prevalence of late ARM (neovascular or atrophic) increased sharply with age, from 3.5 % and 1.8 % in men and women aged 73 to 79 years, to 6.8 % and 10.4 % in men and women aged 80 years or more, respectively. Neovascular ARM represented 25 of 49 cases of late ARM (51 %). Early ARM (1 or 2) was present in 23.3 % and 31.5 % of men and women, respectively. The prevalence of early ARM 1 and 2 increased moderately with age, with early ARM 2 representing about one third of early ARM cases.

Retinopathy was present in at least one eye of 9.1 % of men and 8.1 % of women.. Twenty five cases of retinopathy occurred in the 115 diabetic subjects (prevalence: 21.7 %, 95 % confidence interval: 14.2 % – 29.4 %), while 40 cases occurred in the 633 non-diabetic subjects (prevalence: 6.3 %, 95 % confidence interval: 4.4 % – 8.2 %). Retinal vein occlusion was found in 1.1 % of men and 1.2 % of women and epiretinal membranes in 6.3 % of men and 2.4 % of women.

Glaucoma could be classified in 936 of 963 participants (97.2 %). The prevalence of open-angle glaucoma increased moderately, from 4.8 % and 3.1 % in men and women aged 73 to 79 years, to 6.0 and 6.1 % of men and women aged 80 years or more. We observed no case of angle closure glaucoma. Seventeen of the 45 glaucoma cases (37.8 %) were previously undiagnosed. In addition, 10.0 % of men and women were currently under therapy for ocular hypertension and 37.1 % of men and 50.2 % of women had had cataract extraction.

The distribution of the features of dry eye disease is presented in Table 3 . As expected, dry eye was more frequent in women, both for self-declared dry eye (34.6 % in women versus 21.8 % in men), current use of artificial tears (21.1 % in women versus 11.3 % in men) and symptomatology (mean OSDI score 24.9 in women versus 17.1 in men). However, tear BUT test was similarly low in women and men (mean 6.8 seconds in women and 6.9 seconds in men). There was a slight increase with age of use of artificial tears and OSDI score, but not of self-declared dry eye or tear BUT.

Discussion

The main strength of this study is that it combines clinical, dietary, biological and genetic information, collected over a 7 year period of time before the first eye examination. This will allow to assess the associations of eye diseases with history of nutritional status (collected prospectively), while taking into account vascular and genetic background. Another strength is the fact that we collected both dietary and blood biomarkers of nutritional status. This may give some important insight into the bioavaibility of nutrients.

A potential limitation to our results would be the questionable representativeness of the sample. Indeed, about two third of the participants in the 3C Study accepted the eye examination. This subsample over-represented subjects of younger age and higher socio-economic status, among subjects participating to the 3C Study, who are themselves imperfectly representative of the general population (27). The included subjects may therefore be healthier and have different lifestyles, in particular concerning diet and physical activity, than the general population. This may in turn affect the distribution of nutritional and vascular characteristics, or the prevalence of eye diseases. However, this appears to have had little impact on the distribution of the parameters of interest in the Alienor study. Indeed, participants were mostly comparable to non participants with regard to nutritional and vascular parameters, after adjustment for age and gender. Among the numerous tested variables, only plasma HDL-cholesterol and triglycerides were significantly different between participants and non participants. Moreover, the prevalence rates of the major ocular end points in participants were very close to those observed in studies performed in similar populations (ARM (33 , 47), glaucoma (48), retinal vein occlusion (49), retinopathy (50 –52), epiretinal membranes (53 –54)), confirming the high prevalence of eye diseases in elderly subjects. With regard to dry eye disease, epidemiological data are particularly scarce, and comparability of studies is low because of differing definitions of dry eye disease. However, the prevalence of all dry eye disease dimensions appear high in the present population, by comparison with previous studies (55 –59). Finally, although the distributions of nutritional and vascular parameters and the prevalence of ocular endpoints may be different from the general population, this is unlikely to bias the estimation of the associations of eye diseases with the vascular and nutritional parameters.

Another potential limitation to this study is the small number of cases for some of the end-points, at least at baseline (late ARM, open-angle glaucoma). However, using the observed distribution of risk factors and endpoints at the first eye examination, and an alpha-level of 5 %, statistical power is at least 80 % for differences of clinical significance in nutritional risk factors (20 % or 30 %), for all end-points.

In conclusion, this study confirms the high prevalence of eye diseases in this sample of French elderly subjects. It will add to the knowledge of the epidemiological associations of nutrition with the risk for eye diseases, in a European cohort study. Such information may help design future interventional studies, in terms of the type of nutritional intervention (dietary and/or supplementation, target nutrients and dose) and of target populations (primary or secondary interventions, high-risk populations based on genetic background or other risk factors, populations with nutrient deficiencies). Future interventional studies might be common with other age-related disorders (cardiovascular disease, dementia, Alzheimer's disease, etc…), because of common nutritional determinants. Finally, this study also includes very complete data on cognition, depressive symptoms, disability and activities of daily living, which will allow the study of the consequences of eye diseases and visual impairment in this sample of French elderly subjects.

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Footnotes:

Declaration of interest: C Delcourt: consultant for Bausch&Lomb, Novartis, Pfizer JF Korobelnik: consultant for Alcon, Novartis, Bayer, Bausch & Lomb, Allergan P Barberger-Gateau: lecture fees for Lesieur, Danone, Bausch & Lomb J Colin: consultant for Addition Technologies Inc, Alcon, Abbott AMO, Optical Express, Horus Pharma, Gene Signal SAS F Malet: consultant for Abbott Medical Optics France, Cibavision. MB Rougier: lecture fees from Zeiss. MN Delyfer, M Le Goff, JF Dartigues: none

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Figure 1

Design of the Alienor Study

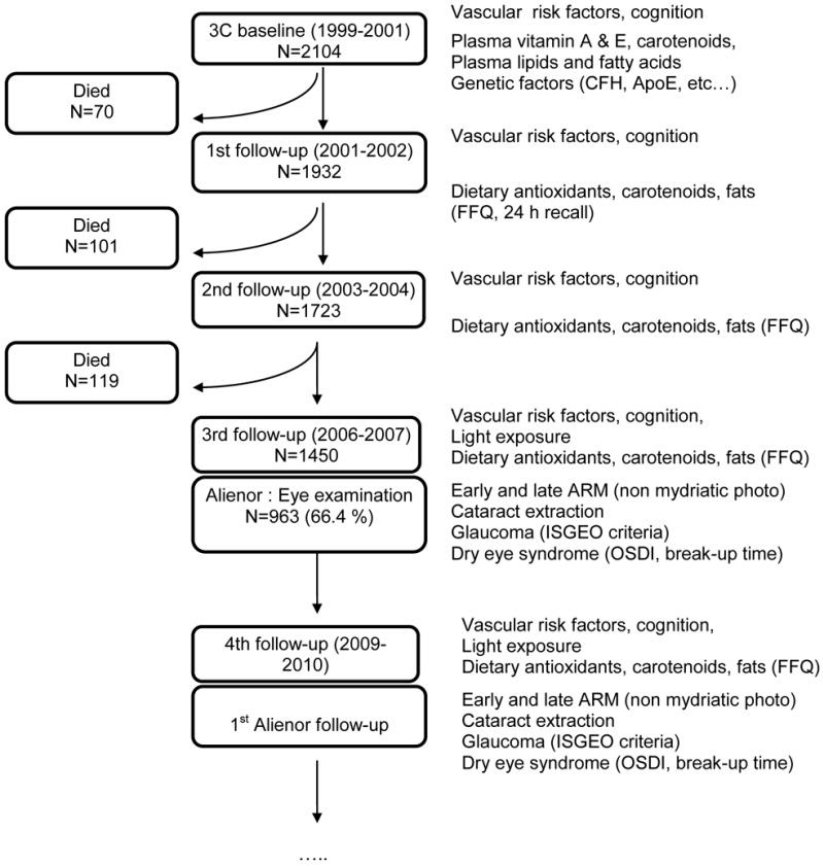

Table 1

Comparison of nutritional status between participants and non participants in the Alienor Study (mean (SD)).

	Participants (n = 963)	**Non participants (n = 487)**	**p-value***
Plasma measurements in 1999–2000	N = 752	N = 354	
Fatty acids (in % of total fatty acids)			
Saturated	39.6 (5.4)	40.2 (5.6)	0.09
Monounsaturated	22.9 (3.7)	23.2 (3.9)	0.48
n-6 PUFA	33.3 (4.9)	32.2 (5.7)	0.06
n-3 PUFA	4.5 (1.3)	4.3 (1.3)	0.07
EPA	1.1 (0.6)	1.0 (0.6)	0.13
DHA	2.5 (0.7)	2.4 (0.8)	0.12
Alpha-tocopherol (mg/l)	15.9 (4.9)	15.7 (5.0)	0.41
Dietary intake from 24h recall in 2001–2002	N=913	N=375	
Energy intake (kcal)	1722 (541)	1627 (558)	0.15
Alcohol (% TEI)	4.9 (5.8)	4.4 (5.4)	0.84
Proteins (% TEI)	18.2 (4.8)	18.2 (4.6)	0.80
Carbohydrates (% TEI)	46.0 (10.1)	46.7 (9.5)	0.50
Total fat (% TEI)	30.9 (8.8)	30.7 (9.1)	0.45
Saturated fat (% TEI)	13.1 (4.7)	13.5 (4.8)	0.66
MUFA (% TEI)	11.1 (4.0)	10.9 (4.0)	0.46
n-6 PUFA (% TEI)	3.4 (2.4)	3.2 (2.1)	0.26
n-3 PUFA (% TEI)	0.6 (0.7)	0.6 (0.6)	0.07
EPA (% TEI)	0.1 (0.2)	0.1 (0.2)	0.15
DHA (% TEI)	0.2 (0.4)	0.1 (0.4)	0.21
Vitamin E (mg/1000 kcal)	3.9 (2.6)	3.7 (2.2)	0.58
Vitamin C (mg/1000 kcal)	53.4 (45.0)	51.6 (43.1)	0.47
Vascular risk factors (in 2006–2008) ** :			
Self-reported history of:			
Hypertension	486 (50.7)	257 (54.8)	0.12
Diabetes	109 (11.4)	62 (13.0)	0.11
Treatment for angina pectoris	77 (8.2)	45 (9.5)	0.99
Myocardial infarction in the last 3 years	10 (1.0)	11 (2.3)	0.11
Stroke in the last 3 years	27 (2.8)	19 (4.0)	0.89
Angioplasty in the last 3 years	31 (3.2)	14 (2.9)	0.97
Smoking			0.11
- never	614 (63.8)	345 (70.9)	
- former	303 (31.4)	115 (23.6)	
- current	46 (4.8)	27 (5.5)	
Body mass index (kg/m^2)	25.9 (4.1)	25.8 (5.0)	0.50
Waist circumference (cm)	91.7 (12.3)	92.3 (13.1)	0.09

Systolic blood pressure (mm Hg)	143.8 (21.4)	143.0 (24.2)	0.22
Diastolic blood pressure (mm Hg)	75.4 (11.0)	74.5 (12.5)	0.59
	N=902	N=408	
Total cholesterol (mmol/l)	5.78 (0.98)	5.81 (0.99)	0.92
LDL-cholesterol (mmol/l)	3.63 (0.85)	3.62 (0.85)	0.76
HDL-cholesterol (mmol/l)	1.59 (0.40)	1.56 (0.41)	0.01
Triglycerides (mmol/l)	1.23 (0.60)	1.37 (0.72)	<0.0001

* adjusted for age and gender using logistic regression

** except for smoking and plasma lipids, which were measured at baseline of the 3C Study (1999–2001)

TEI: total energy intake

Table 2

Prevalence of major eye diseases in the Alienor sample (2006–2008) (% [95% confidence interval])

	73–79 years	≥ 80 years	Total
Men			
Age-related maculopathy	N=198	N=133	N=331
Late neovascular ARM	1.0 [0.1 ; 3.6]	2.3 [0.5 ; 6.6]	1.5 [0.2 ; 2.9]
Late atrophic ARM	2.5 [0.8 ; 5.8]	4.5 [1.7 ; 9.8]	3.3 [1.8 ; 6.5]
Early ARM 2	6.1 [2.8 ; 9.4]	9.8 [4.7 ; 14.9]	7.6 [4.7 ; 10.5]
Early ARM 1	14.6 [9.7 ; 19.5]	17.3 [10.9 ; 23.7]	15.7 [11.8 ; 19.6]
Large drusen	11.1 [6.7 ; 15.5]	18.8 [12.2 ; 25.4]	14.2 [10.4 ; 18.0]
Pigmentary abnormalities	16.2 [11.1 ; 21.3]	24.8 [17.5 ; 32.1]	19.6 [15.3 ; 23.9]
Other retinal diseases	N=198	N=133	N=331
Retinopathy	6.6 [3.1 ; 10.1]	12.8 [7.1 ; 18.5]	9.1 [6.0 ; 12.2]
Retinal vein occlusion	1.5 [0.3 ; 4.3]	0.8 [0.0 ; 4.2]	1.2 [0.4 ; 3.4]
Epiretinal membrane (preretinal fibrosis)	8.6 [4.7 ; 12.5]	3.0 [0.8 ; 7.7]	6.3 [3.7 ; 8.9]
Open-angle Glaucoma	N = 210	N = 148	N = 358
	4.8 [2.4 ; 9.0]	6.1 [2.8 ; 11.1]	5.3 [3.0 ; 7.6]
Treatment for ocular hypertension	N = 214	N = 153	N = 367
	10.3 [6.2 ; 14.4]	9.2 [4.6 ; 13.8]	9.8 [6.7 ; 12.9]
Cataract extraction	N = 211	N = 153	N = 364
	22.8 [17.1 ; 28.5]	56.9 [49.1 ; 64.7]	37.1 [32.1 ; 42.1]
Women			
Age-related maculopathy	N=280	N=268	N=548
Late neovascular ARM	1.1 [0.2 ; 2.9]	6.3 [3.4 ; 9.2]	3.6 [2.0 ; 5.2]
Late atrophic ARM	0.7 [0.1 ; 2.4]	4.1 [2.2 ; 7.7]	2.4 [1.1 ; 3.7]
Early ARM 2	13.2 [9.2 ; 17.2]	11.2 [7.4 ; 15.0]	12.2 [9.5 ; 14.9]
Early ARM 1	16.8 [12.4 ; 21.2]	22.0 [17.0 ; 27.0]	19.3 [16.0 ; 22.6]
Large drusen	18.6 [14.0 ; 23.2]	19.9 [15.1 ; 24.7]	19.2 [15.9 ; 22.5]
Pigmentary abnormalities	18.6 [14.0 ; 23.2]	27.4 [22.1 ; 32.7]	22.9 [19.4 ; 26.4]
Other retinal diseases	N=280	N=266	N=546
Retinopathy	6.1 [3.3 ; 8.9]	10.2 [6.6 ; 13.8]	8.1 [5.8 ; 10.4]
Retinal vein occlusion	0.7 [0.1 ; 2.4]	1.5 [0.4 ; 4.0]	1.1 [0.4 ; 2.6]
Epiretinal membrane (preretinal fibrosis)	3.6 [1.4 ; 5.8]	1.1 [0.2 ; 3.5]	2.4 [1.1 ; 3.7]
Open-angle Glaucoma	N = 293	N = 285	N = 578
	3.1 [1.4 ; 5.6]	6.0 [3.2 ; 8.8]	4.5 [2.8 ; 6.2]
Treatment for ocular hypertension	N = 297	N = 299	N = 596
	12.1 [8.4 ; 15.8]	8.0 [4.9 ; 11.1]	10.1 [7.7 ; 12.5]
Cataract extraction	N = 297	N = 297	N = 594
	37.4 [31.9 ; 42.9]	63.0 [57.5 ; 68.5]	50.2 [46.2 ; 54.2]

Table 3

Distribution of features of dry eye in the Alienor sample (2006–2008) (% [95% confidence interval] or mean (standard deviation))

	73–79 years	≥ 80 years	Total
Men	N = 207	N = 147	N = 354
Self-declared dry eye (%)	24.2 [18.4 – 30.0]	18.4 [13.1 – 24.7]	21.8 [17.5 – 26.1]
Current use of artificial tears (%)	10.1 [6.0 – 14.2]	12.9 [7.5 – 18.3]	11.3 [8.0 – 14.6]
Ocular Surface Disease Index (points)	15.1 (16.7)	20.0 (17.9)	17.1 (17.4)
	N = 188	N = 134	N = 322
Tear break-up time test (seconds)	7.0 (3.1)	6.7 (2.9)	6.9 (3.0)
Women	N = 282	N = 278	N = 560
Self-declared dry eye (%)	35.5 [29.9 – 41.1]	33.8 [28.2 – 39.4]	34.6 [30.7 – 38.5]
Current use of artificial tears (%)	19.5 [14.9 – 24.1]	22.7 [17.8– 27.6]	21.1 [17.7 – 24.5]
Ocular Surface Disease Index (points)	22.7 (21.2)	27.1 (24.8)	24.9 (23.1)
	N = 232	N = 234	N = 466
Tear break-up time test (seconds)	7.0 (2.7)	6.7 (2.6)	6.8 (2.7)