E.2 Risk factors

E.2.1 Risk factors for development or progression of AMD

RQ2: What risk factors increase the likelihood of a person developing AMD or progressing to late AMD?

Bibliographic reference	Risk factors for choroidal neovascularization in the second eye of patients with juxtafoveal or subfoveal choroidal neovascularization secondary to age-related macular degeneration. Macular Photocoagulation Study Group, Archives of ophthalmology (Chicago, Ill.: 1960), 115, 741-747, 1997
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To verify and quantify previously reported risk factors for the development of choroidal neovascularisation in the fellow eye of patients with 1 eye affected with CNV secondary to age-related macular degeneration.
Study dates	Published 1997 Enrolled between 1981 and 1990 for 5 years follow up
Source of funding	Support was given through National Eye Institute, National Institutes of Health and Research to Prevent Blindness
Number of patients	670 patients with unilateral CNV secondary to AMD
Inclusion Criteria	Included in the Macular Photocoagulation Study Group randomised trial of laser photocoagulation for new juxtafoveal choroidal neovascularisation (CNV), new subfoveal CNV or recurrent subfoveal CNV secondary to age related macular degeneration (AMD). Visual acuity of 20/400 or better in the study eye No restrictions on the morphological features or visual acuity of the fellow eye Only fellow eyes without CNV at enrolment were examined for characteristics of drusen and the retinal pigment epithelium.
Exclusion Criteria	Fellow eyes with missing or uninterpretable photographs at enrolment were excluded (n=21). Eyes with some missing photographs or poor quality photographs could not be graded for some features were excluded from analysis on a feature specific basis.
Diagnostic criteria	Systemic hypertension status was classified as normal (systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg in the absence of antihypertensive medications, definite (systolic blood pressure >= 160 mm Hg or diastolic blood

Bibliographic reference	Risk factors for choroidal neovascularization in the second eye of patients with juxtafoveal or subfoveal choroidal neovascularization secondary to age-related macular degeneration. Macular Photocoagulation Study Group, Archives of ophthalmology (Chicago, Ill.: 1960), 115, 741-747, 1997
	pressure >=95 mm Hg, or use of antihypertensive medication), or suspect (systolic blood pressure >=140 but <160 mm Hg or diastolic blood pressure >=95 mmHg but <95 mm Hg in the absence of antihypertensive medication. At each follow up visit stereoscopic colour photographs were taken of the macula of each eye. Fluorescein angiography was performed 3 and 12 months after enrolment and annually thereafter. If CNV in the fellow eye was suggested by signs or symptoms, the macula of the fellow eye was photographed during the fluorescein angiogram. All investigations were assessed independently by 2 readers. Discrepancies that could not be resolved by the two were reviewed for final resolution by an ophthalmologist.
Patient characteristics	Total (n=670) Age, y, no. 50-69: 237 70-74: 168 ≥75: 265 Gender, no. Female: 371 Male: 299 Ethnicity: not reported.
Predictors/risk factors and effect estimates	Risk factors under study included presence of 5 or more drusen, focal hyperpigmentation, definite systemic hypertension, 1 or more large drusen, medication status and blood pressure status of patients with definite hypertension were included in the analysis.
Outcomes	Risk ratios for development of choroidal neovascularisation in the fellow eye of people with choroidal neovascularisation secondary to AMD
Analysis used	Cox proportional hazard analysis
Length of follow up	Follow up visits 3 and 6 months after enrolment and at 6 months intervals thereafter until 5 years follow up.

Bibliographic reference	Risk factors for choroidal neovascularization in the second eye of patients with juxtafoveal or subfoveal choroidal neovascularization secondary to age-related macular degeneration. Macular Photocoagulation Study Group, Archives of ophthalmology (Chicago, Ill.: 1960), 115, 741-747, 1997
Missing data handling/loss to follow up	Fellow eyes with missing or uninterpretable photographs at enrolment were excluded (n=21). Eyes with some missing photographs or poor quality photographs could not be graded for some features were excluded from analysis on a feature specific basis. Complete information on development of CNV within 5 years was available for 408 patients (61%). 73 patients had died or had their follow up period terminated before 3 years, 66 before 4 years and an additional 123 before 5 years. Fundus photograph reading centre gradings of the central macular zone were available for 485 patients (fellow eyes of patients assigned to observation in the clinical trial for juxtafoveal CNV were not examined)
Results	Risk of development of choroidal neovascularisation in the fellow eye of people with choroidal neovascularisation secondary to AMD. Risk ratios (95% confidence intervals): Presence of 5 or more drusen: 2.1 (1.3-3.5) Focal hyperpigmentation: 2.0 (1.4-2.9) Definite systemic hypertension: 1.7 (1.2-2.4) 1 or more large drusen: 1.5 (1.0-2.2) Medication status and blood pressure status of patients with definite hypertension did not influence significantly the incidence of CNV after adjustment for the other factors.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE

Bibliographic reference	**Risk factors for choroidal neovascularization in the second eye of patients with juxtafoveal or subfoveal choroidal neovascularization secondary to age-related macular degeneration. Macular Photocoagulation Study Group, Archives of ophthalmology (Chicago, Ill.: 1960), 115, 741-747, 1997**
	Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). NO Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Ajani,U.A., Christen,W.G., Manson,J.E., Glynn,R.J., Schaumberg,D., Buring,J.E., Hennekens,C.H., A prospective study of alcohol consumption and the risk of age-related macular degeneration, Annals of epidemiology, 9, 172-177, 1999**
Country/ies where the study was carried out	USA Data taken from the Physicians Health Study
Study type	Prospective prognostic study using data from a randomised controlled trial
Aim of the study	To examine the relationship between alcohol intake and development of AMD
Study dates	Published 1999
Source of funding	Supported by National Institutes of Health Grants
Number of patients	A total of 21,041 male physicians
Inclusion Criteria	Male physicians aged between 40-84 years at entry Physicians Health Study was a randomised double blind placebo controlled trial of aspirin (325 mg on alternate days) and beta-carotene (50 mg on alternate days) in the primary prevention of cardiovascular disease and cancer in 1982.

Bibliographic reference	**Ajani,U.A., Christen,W.G., Manson,J.E., Glynn,R.J., Schaumberg,D., Buring,J.E., Hennekens,C.H., A prospective study of alcohol consumption and the risk of age-related macular degeneration, Annals of epidemiology, 9, 172-177, 1999**
	• Inclusion criteria from the original trial: • Ability to give true informed consent • Knowledge of possible side effects • Accuracy and completeness of information • Ease of follow-up • Opportunity to conduct trial by mail
Exclusion Criteria	Exclusion criteria from the original trial: • Personal history of Myocardial infarction, Stroke or TIA, Cancer (except non-melanoma skin cancer), Current liver or kidney disease, Peptic ulcer or gout • Contraindication to aspirin use • Current use of aspirin or other drugs affecting platelet function • Current use of vitamin A or beta-carotene supplement
Diagnostic criteria	Any AMD was defined as a self-report confirmed by a medical record review of an initial diagnosis of AMD subsequent to randomisation AMD with vision loss was defined as above but with vision loss to 20/30 or worse attributable to AMD Exudative AMD was defined by the presence of RPE detachment, subretinal neovascular membrane, or disciform scar.
Patient characteristics	Ethnic group, mean (standard deviation): Not recorded Age, mean (standard deviation): 53.2 (9.5) Gender, mean (standard deviation): male (100%)
Predictors/risk factors and effect estimates	Crude estimates of association were derived by adjusting for effects of age The following factors were adjusted for within the model, age, randomised treatment assignment (aspirin and beta carotene), history of diabetes, history of hypertension, history of treatment for high blood pressure, obesity, physical activity, parental history of myocardial infarction before age 60, smoking status at baseline, multivitamin use at baseline, pack years of smoking. Additional models with updated alcohol data were also run to assess the time varying effect of alcohol.
Outcomes	Individuals rather than eyes were the unit of analysis.

Bibliographic reference	**Ajani,U.A., Christen,W.G., Manson,J.E., Glynn,R.J., Schaumberg,D., Buring,J.E., Hennekens,C.H., A prospective study of alcohol consumption and the risk of age-related macular degeneration, Annals of epidemiology, 9, 172-177, 1999**
	Relative risk of AMD (any kind), AMD with vision loss and exudative AMD with time varying analysis, split by 5 levels of alcohol intake: • <1 drink/week • 1 drink/week • 2-4 drinks/week • 5-6 drinks/week • ≥1 drink/day
Analysis used	Cox proportional hazard models were used to assess the independent contribution of alcohol consumption to the risk of AMD.
Length of follow up	12 years follow up
Missing data handling/loss to follow up	All recorded baseline variables appear to have been entered into the multivariable model Of 22,071 US male physicians at study entry, a total of 21,041 with complete data on alcohol use and no AMD at baseline were entered into the analysis.
Results	Adjusted relative risk for any AMD diagnosis (95% confidence intervals): • <1 drink/week- 1.0 (referent) • 1 drink/week- 0.92 (0.65-1.30) • 2-4 drinks/week- 0.70 (0.51-0.97) • 5-6 drinks/week- 1.25 (0.92-1.71) • ≥1 drink/day- 1.23 (0.96-1.57) Adjusted relative risk for exudative AMD (95% confidence intervals): • <1 drink/week- 1.0 (referent) • 1 drink/week- 1.12 (0.47-2.68) • 2-4 drinks/week- 0.88 (0.39-1.96) • 5-6 drinks/week- 1.20 (0.52- 2.78)

Bibliographic reference	**Ajani,U.A., Christen,W.G., Manson,J.E., Glynn,R.J., Schaumberg,D., Buring,J.E., Hennekens,C.H., A prospective study of alcohol consumption and the risk of age-related macular degeneration, Annals of epidemiology, 9, 172-177, 1999**
	• ≥1 drink/day- 1.33 (0.70-2.50)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). PARTLY Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNCLEAR Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

<table>
<tr><th>Bibliographic reference</th><th>Boekhoorn,Sharmila S., Vingerling,Johannes R., Hofman,Albert, de Jong,Paulus T.V.M., Alcohol consumption and risk of aging macula disorder in a general population: the Rotterdam Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 834-839, 2008</th></tr>
<tr><td>Country/ies where the study was carried out</td><td>The Netherlands</td></tr>
<tr><td>Study type</td><td>Prospective, population-based cohort</td></tr>
<tr><td>Aim of the study</td><td>To investigate the possible relationship between overall alcohol consumption and risk of AMD in a general population
The Rotterdam Study included cardiovascular, locomotor, neurologic and ophthalmologic diseases in those ≥55years</td></tr>
<tr><td>Study dates</td><td>March 1990 to December 2004</td></tr>
<tr><td>Source of funding</td><td>Unrestricted grant from Topcon EuropeBV, Capelle aan de Ijssel</td></tr>
<tr><td>Number of patients</td><td>N=4229 with data on alcohol consumption (67.0% of those with gradable fundus transparencies at baseline)</td></tr>
<tr><td>Inclusion Criteria</td><td>All inhabitants ≥55years living in a suburb of Rotterdam</td></tr>
<tr><td>Exclusion Criteria</td><td>None</td></tr>
<tr><td>Diagnostic criteria</td><td>Diagnosis of AMD, 35mm-colour photographs, graded using x12.5 magnification according to the International Classification and Grading System for Age-Related Maculopathy and Age-Related Macular Degeneration (graded by 2 graders with 11years experience). Divided into early and late AMD
Grading procedures and definitions, and graders, identical at baseline and follow-up</td></tr>
<tr><td>Patient characteristics</td><td>Baseline characteristics
<table>
<tr><td></td><td>No iAMD</td><td>early iAMD</td><td>late iAMD</td></tr>
<tr><td>Age (mean, SD)</td><td>66.3 (7.2)</td><td>68.0 (7.1)</td><td>71.3 (6.4)</td></tr>
<tr><td>Female sex (no. %)</td><td>2166 (59.7)</td><td>295 (56.8)</td><td>49 (60.5)</td></tr>
<tr><td>Alcohol consumption, 0 (no.%)</td><td>704 (19.4)</td><td>90 (17.3)</td><td>15 (18.5)</td></tr>
<tr><td>Alcohol consumption, ≤10g</td><td>1638 (45.1)</td><td>235 (45.3)</td><td>37 (45.7)</td></tr>
<tr><td>Alcohol consumption, >10 to ≤20g</td><td>568 (15.7)</td><td>82 (15.8)</td><td>11 (13.6)</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>Bibliographic reference</th><td colspan="4">Boekhoorn,Sharmila S., Vingerling,Johannes R., Hofman,Albert, de Jong,Paulus T.V.M., Alcohol consumption and risk of aging macula disorder in a general population: the Rotterdam Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 834-839, 2008</td></tr>
<tr><td></td><td colspan="4"><table>
<tr><td>Alcohol consumption, >20g</td><td>719 (19.8)</td><td>112 (21.6)</td><td>18 (22.2)</td></tr>
</table></td></tr>
<tr><td>Predictors/risk factors and effect estimates</td><td colspan="4">Alcohol consumption:
Checklist provided prior to baseline examinations; reported alcohol consumed on a weekly basis in 4 categories (beer, wine, liquor, moderately strong alcoholic beverages)
Total alcohol per participant (in grams)/day calculated
Daily alcohol categorised (0, ≤10g, >10g but ≤20g, >20g)
Potential confounders collected; smoking habits, BP, BMI, total cholesterol, lipids, complement factor H genotypes</td></tr>
<tr><td>Analysis used</td><td colspan="4">Cox proportional hazards regression model</td></tr>
<tr><td>Length of follow up</td><td colspan="4">Mean time baseline to first follow-up 2.0years
Mean time baseline to second follow-up 6.5years
Mean time baseline to third follow-up 11.1years</td></tr>
<tr><td>Missing data handling/loss to follow up</td><td colspan="4">Some data on alcohol consumption unavailable for analysis due to inconsistencies in dietary interviews</td></tr>
<tr><td>Results</td><td colspan="4">Results:
Risk of early or late iAMD, according to alcohol consumption<table>
<tr><td>alcohol, g</td><td>Total no. of participants</td><td>No. of cases</td><td>HR (95%CI)*</td><td>HR (95%CI)#</td></tr>
<tr><td>early iAMD</td><td></td><td></td><td></td><td></td></tr>
<tr><td>0</td><td>794</td><td>90</td><td>1 (ref)</td><td>1 (ref)</td></tr>
<tr><td>≤10</td><td>1873</td><td>235</td><td>1.01 (0.79 to 1.29)</td><td>1.00 (0.76 to 1.30)</td></tr>
<tr><td>>10 to ≤20</td><td>650</td><td>82</td><td>1.04 (0.76 to 1.40)</td><td>0.98 (0.70 to 1.36)</td></tr>
<tr><td>>20</td><td>831</td><td>112</td><td>1.11 (0.83 to 1.48)</td><td>1.10 (0.80 to 1.51)</td></tr>
</table></td></tr>
</table>

Bibliographic reference	**Boekhoorn,Sharmila S., Vingerling,Johannes R., Hofman,Albert, de Jong,Paulus T.V.M., Alcohol consumption and risk of aging macula disorder in a general population: the Rotterdam Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 834-839, 2008**

late iAMD				
0	719	15	1 (ref)	1 (ref)
≤10	1675	37	0.94 (0.51 to 1.72)	1.00 (0.53 to 1.89)
>10 to ≤20	579	11	0.94 (0.43 to 2.08)	0.77 (0.33 to 1.80)
>20	737	18	1.26 (0.61 to 2.60)	1.01 (0.46 to 2.21)

*adjusted for age and sex
#also adjusted for smoking, BMI, BP, complement H factor genotype status, total cholesterol, HDL cholesterol

Risk of dry or wet late iAMD, according to alcohol consumption

alcohol, g	Total no. of participants	No. of cases	HR (95%CI)*	HR (95%CI)
Dry late iAMD				
0	708	4	1 (ref)	1 (ref)
≤10	1648	10	0.93 (0.29 to 2.99)	1.10 (0.32 to 3.80)
>10 to ≤20	573	5	1.58 (0.42 to 6.04)	1.38 (0.31 to 6.16)
>20	731	12	3.09 (0.93 to 10.27)	3.27 (0.88 to 12.19)
Wet late iAMD				
0	715	11	1 (ref)	1 (ref)
≤10	1665	27	0.95 (0.47 to 1.92)	0.96 (0.45 to 2.03)

Bibliographic reference	**Boekhoorn,Sharmila S., Vingerling,Johannes R., Hofman,Albert, de Jong,Paulus T.V.M., Alcohol consumption and risk of aging macula disorder in a general population: the Rotterdam Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 834-839, 2008**

>10 to ≤20	574	6	0.71 (0.26 to 1.96)	0.60 (0.21 to 1.72)
>20	725	6	0.59 (0.21 to 1.68)	0.40 (0.13 to 1.25)

*adjusted for age and sex
#also adjusted for smoking, BMI, BP, complement H factor genotype status, total cholesterol, HDL cholesterol

Risk of early or late iAMD, according to alcohol consumption of different types, adjusted for age and sex

	early iAMD			late iAMD		
	Total	No. of cases	HR (95%CI)	Total	No. of cases	HR (95%CI)
Beer, 0g	794	90	1 (ref)	719	15	1 (ref)
≤10	598	69	0.79 (0.53 to 1.15)	536	7	0.63 (0.20 to 1.98)
>10 to ≤20	95	8	0.66 (0.31 to 1.41)	88	1	0.82 (0.09 to 7.20)
>20	74	12	1.28 (0.66 to 2.48)	64	2	1.94 (0.35 to 10.67)
Wine, 0g	794	90	1 (ref)	719	15	1 (ref)
≤10	1738	214	0.99 (0.78 to 1.27)	1562	38	1.04 (0.57 to 1.89)
0	377	51	1.18 (0.83 to 1.67)	334	8	1.39 (0.58 to 3.32)
>20	235	35	1.32 (0.89 to 1.96)	202	2	0.60 (0.13 to 2.63)
Liquor, 0g	794	90	1 (ref)	719	15	1 (ref)
≤10	740	94	0.90 (0.66 to 1.23)	655	9	0.45 (0.18 to 1.11)

Bibliographic reference	**Boekhoorn,Sharmila S., Vingerling,Johannes R., Hofman,Albert, de Jong,Paulus T.V.M., Alcohol consumption and risk of aging macula disorder in a general population: the Rotterdam Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 834-839, 2008**

>10 to ≤20	291	34	0.81 (0.54 to 1.23)	264	7	0.92 (0.35 to 2.44)
>20	435	56	0.92 (0.64 to 1.33)	389	10	0.98 (0.40 to 2.40)

*adjusted for age 435and sex

#adjusted for smoking, BMI, BP, complement H factor genotype status, total cholesterol, HDL cholesterol

Limitations	The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNCLEAR Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNCLEAR Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Bressler, S. B., Maguire,M.G., Bressler,N.M., Fine,S.L., Relationship of drusen and abnormalities of the retinal pigment epithelium to the prognosis of neovascular macular degeneration. The Macular Photocoagulation Study Group, Archives of ophthalmology (Chicago, Ill.: 1960), 108, 1442-1447, 1990**
Country/ies where the study was carried out	USA
Study type	Prospective cohort
Aim of the study	To describe the relationship of drusen and abnormalities of the retinal pigment epithelium to the prognosis of neovascular AMD in the fellow eye of people diagnosed with neovascular AMD.
Study dates	Published 1990
Source of funding	Grants from the National Eye Institute and National institutes of Health.
Number of patients	127 participants were included in the analysis
Inclusion Criteria	• Diagnosis of choroidal neovascularisation associated with macular degeneration • The posterior edge of the neovascular membrane was to be between 200 and 2500 µm from the foveal center. • Fellow eye with no evidence of neovascular AMD
Exclusion Criteria	• Ungradable or missing photographs at study entry
Diagnostic criteria	The development of the neovascular or exudative form of AMD in the fellow eye was determined by prospective assessment of fundus photographs and fluorescein angiography. All study patients had colour fundus photographs and of the fellow eye submitted at study entry, at 3 months and then semi-annually for 5 years. The same intervals were used for fluorescein angiography except these were taken annually for 5 years. The neovascular form of AMD was considered present whenever hyperfluorescent leakage, a disciform scar, or a laser scar from follow up fluorescein angiogram was observed. A masked review of the follow up colour fundus photographs was performed.
Patient characteristics	No information regarding patient demographics was described
Predictors/risk factors and effect estimates	Variables under study included large drusen, confluent drusen, hyperpigmentation, cigarette smoking and hypertension. Unclear which other variables were adjusted for within the life table analysis
Outcomes	Risk of developing incident neovascular disease in the fellow eye
Analysis used	Multivariate life-table analysis

Bibliographic reference	**Bressler, S. B., Maguire,M.G., Bressler,N.M., Fine,S.L., Relationship of drusen and abnormalities of the retinal pigment epithelium to the prognosis of neovascular macular degeneration. The Macular Photocoagulation Study Group, Archives of ophthalmology (Chicago, Ill.: 1960), 108, 1442-1447, 1990**
Length of follow up	Up to 5 years
Missing data handling/loss to follow up	5 years of follow up was completed for 180 of the 208 patients still alive after 5 years in the Study of the Macular Photocoagulation Study and Senile Macular Degeneration Study. No further information described regarding missing information for the 127 patients included in the analysis
Results	Multivariate analysis of the risk for incident neovascular AMD in the fellow eye, relative risk, (95% confidence intervals): • No large drusen: 1.00 (referent) • large drusen (≥50µm): 2.4 (1.1-5.1) • No focal hyperpigmentation: 1.00 (referent) • Focal hyperpigmentation: 2.5 (1.3-4.9) • No confluent drusen: 1.00 (referent) • Confluent drusen: 1.8 (0.8-3.9) Unclear which other variables were entered into the cox proportional hazards model. Definite hypertension, cigarette smoking and age were not found to influence the risk of developing neovascular AMD.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE

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	Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). UNSURE The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Chew,E.Y., Sperduto,R.D., Milton,R.C., Clemons,T.E., Gensler,G.R., Bressler,S.B., Klein,R., Klein,B.E., Ferris,F.L.,III, 20090213, Risk of advanced age-related macular degeneration after cataract surgery in the Age-Related Eye Disease Study: AREDS report 25, Ophthalmology, 116, 297-303, 2009**
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To assess the risk of developing advanced age-related macular degeneration (AMD) following cataract surgery
Study dates	Published 2009 Enrolled from 1992 through 1998, follow up until 2004.

Bibliographic reference	**Chew,E.Y., Sperduto,R.D., Milton,R.C., Clemons,T.E., Gensler,G.R., Bressler,S.B., Klein,R., Klein,B.E., Ferris,F.L.,III, 20090213, Risk of advanced age-related macular degeneration after cataract surgery in the Age-Related Eye Disease Study: AREDS report 25, Ophthalmology, 116, 297-303, 2009**
Source of funding	Supported by contracts from the National Eye Institute, National Institutes of Health, Department of Health and Human Services.
Number of patients	2880 right eyes and 2961 left eyes
Inclusion Criteria	• 55 to 80 years of age at enrolment • Best-corrected visual acuity (BCVA) of 20/32 or better in at least one eye (the study eye). • Media had to be sufficiently clear to obtain adequate quality stereoscopic fundus photographs of the macula in all study eyes.
Exclusion Criteria	• Eyes with cataract surgery or advanced AMD at baseline. • Patients within "category 1" were excluded from the cox proportional hazards regression analysis. [see diagnostic criteria] • Persons aged 55 to 59 years were eligible for the study only if they were in Category 3 or 4. [see diagnostic criteria]=
Diagnostic criteria	**Definitions of patient categories for cox proportional hazards regression analysis:** Category 1: a total drusen area of less than 5 small drusen (< 63 µm in diameter), and VA of 20/32 or better in both eyes. Category 2: mild age-related macular lesions (multiple small drusen, non-extensive (<20) intermediate drusen (63–124 µm in diameter), pigment abnormalities, or any combination of these) in their most advanced eye, and visual acuity of 20/32 or better in both eyes. Category 3: absence of advanced AMD in both eyes and at least 1 eye with VA of 20/32 or better with at least 1 large druse (≥125 µm in diameter), extensive (as measured by drusen area) intermediate drusen, or geographic atrophy (GA) that did not involve the centre of the macula, or any combination of these. Category 3a: both eyes met these criteria, while in Category 3b one eye had either reduced VA not due to AMD or a disqualifying ocular condition. Category 4: participants had VA of 20/32 or better and no advanced AMD (GA involving the centre of the macula or features of choroidal neovascularization) in the study eye, and the fellow eye had either lesions of advanced AMD (Category 4a) or VA less than 20/32 and AMD abnormalities sufficient to explain reduced VA (Category 4b) as determined by examination of photographs at the reading centre. Only patient categories 2, 3 and 4 were entered into the cox analysis. Persons aged 55 to 59 years were eligible for the study only if they were in Category 3 or 4. Eyes were excluded from this analysis if they were pseudophakic/aphakic or had advanced AMD at baseline.

Bibliographic reference	**Chew,E.Y., Sperduto,R.D., Milton,R.C., Clemons,T.E., Gensler,G.R., Bressler,S.B., Klein,R., Klein,B.E., Ferris,F.L.,III, 20090213, Risk of advanced age-related macular degeneration after cataract surgery in the Age-Related Eye Disease Study: AREDS report 25, Ophthalmology, 116, 297-303, 2009**
	Recording covariates: Questionnaires were administered to obtain demographic information, history of smoking and sunlight exposure, medical history, history of specific prescription drug and non-prescription medication use, and history of vitamin and mineral use. General physical and ophthalmic examinations included height, weight, blood pressure, manifest refraction, best corrected visual acuity, intraocular pressure, slit-lamp biomicroscopy, and ophthalmoscopy. Date of cataract surgery was obtained by history at 6-month intervals. Stereoscopic film-based colour fundus photographs of the macula and lens photographs (red reflex, slit lamp and Neitz) were taken at baseline and annually beginning at the 2 year annual study visit. Photographs were graded at a reading centre, where the various lesions associated with AMD and the severity of lens opacities by type were assessed with standardized grading procedures. **Outcomes** Progression to neovascular AMD for a study eye was based on clinical centre reports of photocoagulation for choroidal neovascularization, or photographic documentation at the reading centre of at least 1 of the following: subretinal fibrosis, non-drusenoid retinal pigment epithelial detachment, serous or haemorrhagic retinal detachment, and haemorrhage under the retina or the retinal pigment epithelium. Progression to geographic atrophy was defined by an area of atrophy >175 um in diameter within the grid to be comparable with previous studies.
Patient characteristics	Total (n=4577) Mean Age, yr (SD): 68 (5) Gender, no. (%) Female: 2555 (56) Male: 2022 (44) Race, no. (%) White: 4374 (96) Other: 203 (4)
Predictors/risk factors and effect estimates	Risk factor under study was incident cataract surgery

Bibliographic reference	Chew,E.Y., Sperduto,R.D., Milton,R.C., Clemons,T.E., Gensler,G.R., Bressler,S.B., Klein,R., Klein,B.E., Ferris,F.L.,III, 20090213, Risk of advanced age-related macular degeneration after cataract surgery in the Age-Related Eye Disease Study: AREDS report 25, Ophthalmology, 116, 297-303, 2009
	Hazard ratios were adjusted for gender and baseline smoking status, as well as time-dependent covariates age, AMD status, and cataract surgery
Outcomes	Hazard ratio for developing neovascular AMD Hazard ratio for developing geographic atrophy
Analysis used	Cox proportional hazards regression analysis
Length of follow up	Every 6 months for up to 11 years (mean follow up 8.8 ± 2.4 years)
Missing data handling/loss to follow up	The study reports low loss to follow up: 2% during the entire clinical trial portion and 4% during the later non-intervention portion of AREDS, not including deaths) and the frequent participant contacts, information on both cataract surgery and progression to advanced AMD was captured for almost all of participants. No further information on missing data was described.
Results	**Hazard ratio for developing neovascular AMD (95% confidence intervals)** Right eye (Category 2,3,4) 1.20 (0.82–1.75) Left eye (Category 2,3,4) 1.07 (0.72–1.58) **Hazard ratio for developing geographic atrophy (95% confidence intervals)** Right eye (Category 2,3,4) 0.80 (0.61–1.06) Left eye (Category 2,3,4) 0.95 (0.71–1.26)

Bibliographic reference	Chew,E.Y., Sperduto,R.D., Milton,R.C., Clemons,T.E., Gensler,G.R., Bressler,S.B., Klein,R., Klein,B.E., Ferris,F.L.,III, 20090213, Risk of advanced age-related macular degeneration after cataract surgery in the Age-Related Eye Disease Study: AREDS report 25, Ophthalmology, 116, 297-303, 2009
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). PARTLY Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). UNSURE Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Chiu,C.-J., Milton,R.C., Klein,R., Gensler,G., Taylor,A., Dietary carbohydrate and the progression of age-related macular degeneration: A prospective study from the Age-Related Eye Disease Study, American Journal of Clinical Nutrition, 86, 1210-1218, 2007**
Country/ies where the study was carried out	USA
Study type	Prospective cohort
Aim of the study	To prospectively evaluate the effect of baseline higher dietary glycaemic index (dGI) on the progression of AMD
Study dates	November 1992 to January 1998
Source of funding	Grants from Johnson and Johnson Focused Giving Program
Number of patients	N=3977 participants (7232 eyes, 722 participants contributed only 1 eye) Number with large drusen or group 3 eyes =2754
Inclusion Criteria	• ≥1 eye with a visual acuity of 20/32 or better, with lens and vitreous sufficiently clear to allow good retinal photographs that would permit identification and quantification of small drusen • ≥1 eye to be free of disease that could complicate assessment of AMD or lens opacity progression, that eye had not had previous ocular surgery
Exclusion Criteria	• Any illness or disorder that would make long-term follow-up or compliance with study protocol unlikely or difficult • Diabetes at baseline • Persons with missing nutritional, non-nutritional, and ophthalmologic covariates • Persons with invalid calorie intake • Persons lost to follow up in the AREDs study • Eyes at the end stage (central Geographic atrophy or neovascular AMD)
Diagnostic criteria	Stereoscopic fundus photographs of the macula graded at an ophthalmic photograph reading centre Lesions associated with AMD assessed according to the AREDS AMD Classification System Eyes classified into 1 of 5 groups according to the size and extent of drusen, presence of geographic atrophy and neovascular changes of AMD
Patient characteristics	Baseline

Characteristic	High dGI	Low dGI

Bibliographic reference	Chiu,C.-J., Milton,R.C., Klein,R., Gensler,G., Taylor,A., Dietary carbohydrate and the progression of age-related macular degeneration: A prospective study from the Age-Related Eye Disease Study, American Journal of Clinical Nutrition, 86, 1210-1218, 2007		
	Age <65yrs, no. (%)	855 (24.15)	901 (24.41)
	Age 65-71 yrs	1428 (40.33)	1485 (40.23)
	Age ≥71yrs	1258 (35.53)	1305 (35.36)
	p2	0.97	
	Race, white, no. (%)	3353 (94.69)	3596 (97.43)
	Race, other	188 (5.31)	95 (2.57)
	p2	<0.001	
	Female, no. (%)	2048 (57.84)	2151 (58.28)
	Male	1493 (42.16)	1540 (41.72)
	p2	0.70	
	Smoking, yes, no. (%)	1925 (54.36)	1931 (52.32)
	Smoking, no	1616 (45.64)	1760 (47.68)
	p2	0.08	
	Alcohol, median	0.89	1.52
	p2	<0.001	
Predictors/risk factors and effect estimates	Comparing high and low dietary glycaemic index in the progression of age related macular degeneration		

Bibliographic reference	**Chiu,C.-J., Milton,R.C., Klein,R., Gensler,G., Taylor,A., Dietary carbohydrate and the progression of age-related macular degeneration: A prospective study from the Age-Related Eye Disease Study, American Journal of Clinical Nutrition, 86, 1210-1218, 2007**
Outcomes	Assessment of daily total carbohydrate calculated by summing the product of the frequency, serving size, and carbohydrate content per serving of individual food items derived from a nutrition database (Nutrition coordinating centre at the University of Minnesota). GI values derived from published values Dose-dependent relationship between dietary glycaemic index and the risk of developing advanced age-related AMD in people with large drusen at baseline, Relative risk (95% confidence intervals)
Analysis used	Cox regression model
Length of follow up	8 years of follow up
Missing data handling/loss to follow up	122 persons lost to follow-up and excluded. People with missing or invalid information were excluded (see exclusion criteria). No further information on missing or incomplete data provided.
Results	Dose-dependent relationship between dietary glycaemic index and the risk of developing advanced age-related AMD in people with large drusen at baseline, Relative risk (95% confidence intervals) (n=2754) Quintile 1: 1.00 (referent) Quintile 2: 1.12 (0.90- 1.40) Quintile 3: 1.14 (0.90-1.44) Quintile 4: 1.20 (1.52-0.94) Quintile 5: 1.39 (1.08-1.79) Cox regression analysis was adjusted for age, sex, race, education, alcohol intake, BMI, hypertension history, refractive error, energy adjusted dietary variables (including total carbohydrates, fat, lutein and zeaxanthin, folic acid, niacin, riboflavin, B-carotene, vitamin C, vitamin E, and zinc intake.)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD;

Bibliographic reference	**Chiu,C.-J., Milton,R.C., Klein,R., Gensler,G., Taylor,A., Dietary carbohydrate and the progression of age-related macular degeneration: A prospective study from the Age-Related Eye Disease Study, American Journal of Clinical Nutrition, 86, 1210-1218, 2007**
	The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Chiu,C.-J., Klein,R., Milton,R.C., Gensler,G., Taylor,A., Does eating particular diets alter the risk of age-related macular degeneration in users of the Age-Related Eye Disease Study supplements?, British Journal of Ophthalmology, 93, 1241-1246, 2009**
Country/ies where the study was carried out	USA
Study type	Prospective cohort (using data from a randomised controlled trial)
Aim of the study	To describe whether enhanced intake of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), and reducing dietary glycaemic index (dGI) are protective against advanced age-related macular degeneration (AMD)

Bibliographic reference	**Chiu,C.-J., Klein,R., Milton,R.C., Gensler,G., Taylor,A., Does eating particular diets alter the risk of age-related macular degeneration in users of the Age-Related Eye Disease Study supplements?, British Journal of Ophthalmology, 93, 1241-1246, 2009**
Study dates	Published 2009 8 year trial period beginning November 13, 1992,
Source of funding	Financial support for this project has been provided by the US Department of Agriculture under agreements, grants from the National Institutes of Health; grants from the Johnson & Johnson Focused Giving Program and American Health Assistance Foundation, and to C-JC from the Ross Aging Initiative.
Number of patients	2924 eligible AREDS AMD trial participants Unit of analysis was the eye (5146 eyes)
Inclusion Criteria	• Participants of the AREDs AMD trial • Eyes at risk of early progression and late progression
Exclusion Criteria	• People with diabetes • Invalid Energy intake • Missing covariates • Advanced AMD at baseline • Lost to follow up
Diagnostic criteria	Data on possible risk factors for AMD were obtained from a baseline general physical and ophthalmic examination, a detailed questionnaire on basic characteristics and demographic data, and a validated food-frequency questionnaire (FFQ). Stereoscopic fundus photographs of the macula were taken and graded at baseline, at the 2-year visit, and annually thereafter during the 8-year (mean: 5.4 years) of follow-up using the AREDS protocol and AMD Classification System. Eyes were classified into one of five groups, numbered serially and based on increasing severity of drusen or type of AMD: Group 1, 2 and 3 defined here as early AMD, and Groups 4 and 5 defined here as advanced AMD. Time to the first maximal AMD progression of studied eyes during the 8-year study period was considered. Progression for a study eye was defined by a more advanced AMD grade than the baseline grade. An ‘‘event’’ of AMD progression was defined as the occurrence of the first maximal AMD progression in one eye at a single visit. The dietary glycaemic index (dGI) for each subject was calculated as the weighted average of the GI values for each food item, with the amount of carbohydrate consumed from each food item as the weight.

Bibliographic reference	**Chiu,C.-J., Klein,R., Milton,R.C., Gensler,G., Taylor,A., Does eating particular diets alter the risk of age-related macular degeneration in users of the Age-Related Eye Disease Study supplements?, British Journal of Ophthalmology, 93, 1241-1246, 2009**
Patient characteristics	Total number of participants(n = 2924) Age in years, mean (SD): 69.3 (4.8) Race, no. (%) White: 2829 (96.8) Others: 95 (3.3) Gender, no. (%) Female 1698 (58.1)
Predictors/risk factors and effect estimates	Risk factors of interest included: Dietary intake of beta-carotene, docosahexanoic acid, eicosapentaenoic acid, and low-glycaemic index. All analyses used eyes as the unit. The multivariate-adjusted hazard ratios (HR) (95% CIs) were calculated using the first quartile group of the nutrient intake as the referent and estimated the global effects of nutrients independent of type of AREDS intervention. The following were considered as covariates in the analyses: age, gender, education level (college or higher, and high school or less), race (white and others), body mass index (BMI, computed from weight and height; kg/m2), smoking status (past, current, and never), alcohol drinking (g/day), sunlight exposure (h/day), hypertension history, baseline AMD classification, presence of lens opacity, refractive error (hyperopic and myopic), Centrum use during the trial period, total calorie intake, and energy adjusted dietary variables including carbohydrate, protein, fat, polyunsaturated fatty acids, arachidonic acid, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), lutein plus zeaxanthin, folic acid, niacin, riboflavin, thiamine, vitamin C, vitamin E, betacarotene and zinc. The p value for interaction evaluated if the association varied by type of AREDS intervention. The four interventions are (1) the full AREDS formulation (vitamin C, vitamin E, beta-carotene and zinc), (2) the AREDS antioxidant formulation (vitamin C, vitamin E and beta-carotene), (3) the AREDS zinc formulation and (4) placebo.
Outcomes	Hazard ratios for the development of early AMD Hazard ratios for the development of late AMD
Analysis used	Cox proportional-hazards models
Length of follow up	8 year follow up

Bibliographic reference	Chiu,C.-J., Klein,R., Milton,R.C., Gensler,G., Taylor,A., Does eating particular diets alter the risk of age-related macular degeneration in users of the Age-Related Eye Disease Study supplements?, British Journal of Ophthalmology, 93, 1241-1246, 2009
Missing data handling/loss to follow up	None described (those with missing data were excluded from analysis)
Results	Associations between dietary intakes and risk of age-related macular degeneration (AMD) Early AMD progression Beta-carotene Quartile (Q) 1: referent Q2 (1.5–2.2 mg/day): 1.02 (0.85 to 1.22) Q3 (2.2–3.2 mg/day): 0.98 (0.80 to 1.18) Q4 (>3.2 mg/day): 0.97 (0.77 to 1.21) Docosahexaenoic acid Q1: referent Q2 (26.0–41.9 mg/day): 1.13 (0.95 to 1.34) Q3 (41.9–64.0 mg/day): 0.98 (0.81 to 1.18) Q4 (>64.0 mg/day): 1.09 (0.88 to 1.35) Eicosapentaenoic acid Q1: referent Q2 (12.7–24.6 mg/day): 1.07 (0.90 to 1.28) Q3 (24.6–42.3 mg/day): 1.01 (0.84 to 1.21) Q4 (>42.3 mg/day): 1.01 (0.83 to 1.23) Low-glycaemic index >81.5: referent 78.6–81.5: 1.15 (0.96 to 1.38) 75.2–78.6: 1.05 (0.87 to 1.28) 75.2: 1.03 (0.83 to 1.29)

Bibliographic reference	**Chiu,C.-J., Klein,R., Milton,R.C., Gensler,G., Taylor,A., Does eating particular diets alter the risk of age-related macular degeneration in users of the Age-Related Eye Disease Study supplements?, British Journal of Ophthalmology, 93, 1241-1246, 2009**
	Late AMD progression Beta-carotene Q1: referent Q2 (1.5–2.2 mg/day): 0.97 (0.80 to 1.19) Q3 (2.2–3.2 mg/day): 1.11 (0.90 to 1.37) Q4 (>3.2 mg/day): 1.24 (0.96 to 1.59) Docosahexaenoic acid Q1: referent Q2 (26.0–41.9 mg/day): 0.97 (0.80 to 1.18) Q3 (41.9–64.0 mg/day): 1.04 (0.85 to 1.28) Q4 (>64.0 mg/day): 0.73 (0.57 to 0.94) Eicosapentaenoic acid Q1: referent Q2 (12.7–24.6 mg/day): 0.91 (0.75 to 1.11) Q3 (24.6–42.3 mg/day): 1.03 (0.85 to 1.24) Q4 (>42.3 mg/day): 0.74 (0.59 to 0.94) Low-glycaemic index >81.5: referent 78.6–81.5: 0.80 (0.67 to 0.97) 75.2–78.6: 0.77 (0.63 to 0.94) 75.2: 0.76 (0.60 to 0.96)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors

Bibliographic reference	**Chiu,C.-J., Klein,R., Milton,R.C., Gensler,G., Taylor,A., Does eating particular diets alter the risk of age-related macular degeneration in users of the Age-Related Eye Disease Study supplements?, British Journal of Ophthalmology, 93, 1241-1246, 2009**
	Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). YES Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Christen,W.G., Glynn,R.J., Ajani,U.A., Schaumberg,D.A., Chew,E.Y., Buring,J.E., Manson,J.E., Hennekens,C.H., Age-related maculopathy in a randomized trial of low-dose aspirin among US physicians, Archives of ophthalmology (Chicago, Ill.: 1960), 119, 1143-1149, 2001**
Country/ies where the study was carried out	USA
Study type	Double masked, Randomised controlled trial

Bibliographic reference	**Christen,W.G., Glynn,R.J., Ajani,U.A., Schaumberg,D.A., Chew,E.Y., Buring,J.E., Manson,J.E., Hennekens,C.H., Age-related maculopathy in a randomized trial of low-dose aspirin among US physicians, Archives of ophthalmology (Chicago, Ill.: 1960), 119, 1143-1149, 2001**
Aim of the study	To examine the development of age-related maculopathy (ARM) in a large-scale trial of low-dose aspirin treatment.
Study dates	Published 2001
Source of funding	Supported by research grants from the National Institutes of Health
Number of patients	22 071 US male physicians 10,617 in the aspirin group and 10,599 in the placebo group
Inclusion Criteria	• Male physicians • Ages 40 to 84 • No history of stroke, myocardial infarction, cancer, or renal disease • No contraindications to aspirin or beta-carotene. • No current usage of aspirin or Vitamin A tables greater than once per week • Followed up for at least 7 years • Did not report Age-related macular degeneration at baseline
Exclusion Criteria	• Physicians who died during the first 7 years of follow-up and therefore did not respond to the 84-month questionnaire were excluded
Diagnostic criteria	Information concerning the occurrence of ARM during the first 7 years of the trial was requested on the 84-month questionnaire. Physicians were asked, "Have you ever had macular degeneration diagnosed in your right (left) eye?" If yes, they were requested to provide the month and year of the diagnosis. Subsequent annual questionnaires requested information on diagnoses during the preceding year. Signed permission to examine medical and hospital records pertaining to the diagnosis was also requested on the questionnaire and in separate follow-up mailings when necessary. Ophthalmologists and optometrists were contacted by mail and asked to complete an ARM questionnaire supplying information about the date of initial diagnosis of ARM, the best-corrected visual acuity at the time of diagnosis, and the date when visual acuity reached 20/30 or worse (if different from the date of initial diagnosis). Information was also requested about the pathological findings observed (drusen, retinal pigment epithelium [RPE] hypopigmentation/hyperpigmentation, geographic atrophy, RPE detachment, subretinal neovascular membrane, or

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	disciform scar) when visual acuity was first noted to be 20/30 or worse and the date when exudative disease was first noted (defined by the presence of RPE detachment, subretinal neovascular membrane, or disciform scar). In addition, they asked whether there were other ocular abnormalities that would explain or contribute to visual loss and, if so, whether the ARM, by itself, was significant enough to cause best-corrected visual acuity to be reduced to 20/30 or worse.
Patient characteristics	Mean age, y (*Aspirin group, **placebo group) Total: *52.8 **52.8 40−49 *42.2 **42.3 50-59 *34.2 **34.1 60-69 *18.0 **17.9 70-84 *5.6 **5.7 Gender: Male Ethnicity: Not reported
Predictors/risk factors and effect estimates	The risk factor of interest was treatment with low-dose aspirin. (325mg of aspirin on alternate days) Models were adjusted for age, and beta carotene treatment assignment.
Outcomes	Risk ratios for the development of any AMD or advanced AMD in those treated with low dose aspirin.
Analysis used	Cox proportional hazards regression
Length of follow up	At least 7 years follow up Aspirin treatment period lasted average of 60.2 months follow up (trial terminated early.
Missing data handling/loss to follow up	No further information provided on missing data
Results	Relative risk of aspirin group vs placebo group for the outcome of development of any incident AMD RR = 0.77 (0.54−1.11)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors

Bibliographic reference	**Christen,W.G., Glynn,R.J., Ajani,U.A., Schaumberg,D.A., Chew,E.Y., Buring,J.E., Manson,J.E., Hennekens,C.H., Age-related maculopathy in a randomized trial of low-dose aspirin among US physicians, Archives of ophthalmology (Chicago, Ill.: 1960), 119, 1143-1149, 2001**
	Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Christen,W.G., Glynn,R.J., Chew,E.Y., Buring,J.E., Low-dose aspirin and medical record-confirmed age-related macular degeneration in a randomized trial of women, Ophthalmology, 116, 2386-2392, 2009**
Country/ies where the study was carried out	USA
Study type	Randomised controlled trial

Bibliographic reference	Christen,W.G., Glynn,R.J., Chew,E.Y., Buring,J.E., Low-dose aspirin and medical record-confirmed age-related macular degeneration in a randomized trial of women, Ophthalmology, 116, 2386-2392, 2009
Aim of the study	To test whether alternate day low-dose aspirin affects incidence of age-related macular degeneration (AMD) in a large-scale randomized trial of women.
Study dates	2009
Source of funding	Supported by research grants from the National Institutes of Health, Bethesda. Md. Pills and packaging were provided by Bayer Healthcare and the Natural Source Vitamin E Association
Number of patients	39,876 female health professionals 19,716 in the aspirin group and 19,705 in the placebo group
Inclusion Criteria	• Healthy women • No previous history of cardiovascular disease or cancer • No contraindications to aspirin or vitamin E • A total of 39,421 women were without a diagnosis of AMD at baseline and are included in these analyses
Exclusion Criteria	None described
Diagnostic criteria	Information on new diagnoses of AMD was requested on annual questionnaires. Participants were asked “In the past year, have you had any of the following?” with response options including “macular degeneration right eye” and “macular degeneration left eye”. If yes, participants were requested to provide the month and year of the diagnosis. Ophthalmologists and optometrists were contacted by mail and requested to complete an AMD questionnaire supplying information about the date of initial diagnosis, the best-corrected visual acuity at the time of diagnosis, and the date when best-corrected visual acuity reached 20/30 or worse (if different from the date of initial diagnosis). Information was also requested about signs of AMD observed. They were also asked whether there were other ocular abnormalities that would explain or contribute to vision loss and if so, whether the AMD, by itself, was significant enough to cause the best-corrected visual acuity to be reduced to 20/30 or worse. Medical records were reviewed without knowledge of treatment assignment. The primary endpoint was visually-significant AMD defined as a self-report confirmed by medical record evidence of an initial diagnosis after randomization but before March 31, 2004, with best corrected vision loss to 20/30 or worse attributable to AMD (not outcomes of interest).

Bibliographic reference	Christen,W.G., Glynn,R.J., Chew,E.Y., Buring,J.E., Low-dose aspirin and medical record-confirmed age-related macular degeneration in a randomized trial of women, Ophthalmology, 116, 2386-2392, 2009
	Two secondary endpoints were: advanced AMD, comprised of those cases of exudative neovascular AMD (defined by presence of RPE detachment, subretinal neovascular membrane, or disciform scar) plus cases of geographic atrophy; and AMD with or without vision loss, comprised of all incident cases confirmed by medical records.
Patient characteristics	Mean age, y (*Aspirin group, **placebo group) Total: *54.5 **54.5 45−54 *60.7 **60.6 55−64 *29.4 **29.4 65+ *9.9 **9.9 Gender: Female Ethnicity: Not reported
Predictors/risk factors and effect estimates	The risk factor of interest was treatment with low-dose aspirin. (100mg of aspirin on alternate days) Models were adjusted for age, vitamin E and beta carotene treatment assignment.
Outcomes	Risk ratios for the development of any AMD or advanced AMD in those treated with low dose asiprin.
Analysis used	Cox proportional hazards regression
Length of follow up	10 years of treatment and follow up
Missing data handling/loss to follow up	Of 19,934 allocated aspirin, 19,716 were included in the analysis. Of 19,942 allocated placebo, 19,705 were included in the analysis.
Results	Relative risk of aspirin group vs placebo group for the outcome of development of advanced AMD RR = 0.90 (0.53−1.52) Relative risk of aspirin group vs placebo group for the outcome of development of AMD (with or without vision loss) RR = 1.03 (0.88−1.21)
Limitations	The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNCLEAR

Bibliographic reference	Christen,W.G., Glynn,R.J., Chew,E.Y., Buring,J.E., Low-dose aspirin and medical record-confirmed age-related macular degeneration in a randomized trial of women, Ophthalmology, 116, 2386-2392, 2009
	Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNCLEAR Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Complications of Age-Related Macular Degeneration Prevention Trial (CAPT) Research Group, 20080911, Risk factors for choroidal neovascularization and geographic atrophy in the complications of age-related macular degeneration prevention trial, Ophthalmology, 115, 1474-1479, 2008.
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To determine risk factors for choroidal neovascularisation and of geographic atrophy in eyes with large drusen
Study dates	Published 2008 Enrolled May 1999 through March 2001, 5 years follow up with 6 month and annual visits
Source of funding	Supported by the National Eye Institute, National Institutes of Health grants.

Bibliographic reference	Complications of Age-Related Macular Degeneration Prevention Trial (CAPT) Research Group, 20080911, Risk factors for choroidal neovascularization and geographic atrophy in the complications of age-related macular degeneration prevention trial, Ophthalmology, 115, 1474-1479, 2008.
Number of patients	1052 participants in a randomised controlled trial of laser treatment for the prevention of vision loss from advanced age-related macular degeneration
Inclusion Criteria	• The presence of 10 or more drusen at least 125um in diameter within 2 disc diameters of the fovea Standardised visual acuity measurement of 20/40 or better in each eye 50 years of age and older Free of conditions likely to preclude 5 years of follow up
Exclusion Criteria	• Evidence of choroidal neovascularisation, serous pigment epithelial detachment, geographic atrophy within 500um of the foveal centre or more than 1 Macular Photocoagulation Study (MPS) disc area. Other ocular conditions that were likely to compromise visual acuity or contraindicate application of laser treatment. CNV, serous epithelial detachment, geographic atrophy at baseline (from the analysis)
Diagnostic criteria	At baseline participants provided a brief medical history. Participants provided information on demographic characteristics, history of diabetes mellitus, history of smoking, current use of aspirin, current use of antihypertensive medication. Blood pressure was measured while patient was sitting. Hypertension was classified according to the BP measured at initial visit and the reported use of antihypertensive medications. Definite hypertension was defined as systolic BP of 95 mmHg or more or current use of antihypertensive medications. Suspect hypertension was defined as either systolic BP of 140 mmHg or more but less than 160 mmHg or diastolic BP of 90 mmHg or more but less than 95 mmHg in participants not taking antihypertensive medications. At initial visit, 6 months and annually thereafter, certified photographers adhering to a standardised protocol obtained stereoscopic funds photographs on film. All photographic images were graded according to the Wisconsin Age-related Maculopathy Grading System and the International Classification and Grading system for Age-related maculopathy and age related macular degeneration. Photographs were graded by 2 readers who later agreed any discrepancies openly to drive at consensus. Fluorescein angiograms were used to identify choroidal neovascularisation defined as expansion or persistent staining of an area of hyper fluorescence as the time from injection increased Geographic atrophy was considered present when the colour photograph showed an area of atrophy of the RPE with a diameter of at least 250um with 2 of the following features: visible choroidal vessels, sharp edges and a more or less circular shape. Endpoint GA was defined as the development of a total of more than 1 MPS disc area of a new, additional atrophy when all areas of GA were within 3000um of the foveal centre were combined.

Bibliographic reference	**Complications of Age-Related Macular Degeneration Prevention Trial (CAPT) Research Group, 20080911, Risk factors for choroidal neovascularization and geographic atrophy in the complications of age-related macular degeneration prevention trial, Ophthalmology, 115, 1474-1479, 2008.**
Patient characteristics	Mean age: 71 years Gender: unclear Ethnicity: 99% white
Predictors/risk factors and effect estimates	Risk factors under analysis included: age, cigarette smoking, hypertension, focal hyper pigmentation, precent of area covered by duress, focal hyper pigmentation, RPE depigmentation. Other risk factors that did not reach significance at univariate level were not entered into the final cox proportional hazards model. Treatment was included as a covariate in this model.
Outcomes	Risk factors for choroidal neovascularisation from multivariate analysis, relative risk (95% confidence intervals) Risk factors for geographic atrophy from multivariate analysis, relative risk (95% confidence intervals)
Analysis used	Cox proportional hazards analysis
Length of follow up	5 years follow up with 6 month and annual visits
Missing data handling/loss to follow up	Through 5 years of follow up, 5891 (97.2%) of visits were completed of the 6061 6 month an annual visits scheduled for surviving CAPT participants in this trial.
Results	**Risk factors for choroidal neovascularisation from multivariate analysis, relative risk (95% confidence intervals)** Age 50-59 years: 1.00 60-69 years: 2.06 (1.06-3.97) 70-79 years: 2.61 (1.39-4.92) >79: 2.81 (1.33-5.94) Cigarette smoking Never: 1.00 Quit: 1.01 (0.76-1.35) Current: 1.98 (1.16-3.39) Hypertension

Bibliographic reference	Complications of Age-Related Macular Degeneration Prevention Trial (CAPT) Research Group, 20080911, Risk factors for choroidal neovascularization and geographic atrophy in the complications of age-related macular degeneration prevention trial, Ophthalmology, 115, 1474-1479, 2008.
	Normal: 1.00 Suspect: 0.69 (0.45-1.07) Definite: 1.23 (0.90-1.68) Focal hyperpigmentation None/questionable: 1.00 <250 um: 1.28 (0.94-1.75) >=250 um: 1.84 (1.22-2.76) **Risk factors for geographic atrophy from multivariate analysis, relative risk (95% confidence intervals)** Age 50-59 years: 1.00 60-69 years: 6.09 (1.72-21.5) 70-79 years: 4.12 (1.18-14.4) >79: 6.39 (1.64-24.9) Hypertension Normal: 1.00 Suspect: 1.01 (0.76-1.35) Definite: 1.98 (1.16-3.39) % of area covered by drusen: <10%: 1.00 10-24%: 2.39 (1.44-3.97) >=25%: 5.10 (2.57-10.1) Focal hyperpigmentation None/questionable: 1.00 <250 um: 2.82 (1.30-6.12) >=250 um: 10.4 (4.51-24.0)

Bibliographic reference	**Complications of Age-Related Macular Degeneration Prevention Trial (CAPT) Research Group, 20080911, Risk factors for choroidal neovascularization and geographic atrophy in the complications of age-related macular degeneration prevention trial, Ophthalmology, 115, 1474-1479, 2008.**
	Retinal pigment epithelium depigmentation: No: 1.00 Yes: 2.64 (1.26-5.53)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). PARTLY Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Finger,Robert P., Wu,Zhichao, Luu,Chi D., Kearney,Frances, Ayton,Lauren N., Lucci,Lucia M., Hubbard,William C., Hageman,Jill L., Hageman,Gregory S., Guymer,Robyn H., Reticular pseudodrusen: a risk factor for geographic atrophy in fellow eyes of individuals with unilateral choroidal neovascularization, Ophthalmology, 121, 1252-1256, 2014**
Country/ies where the study was carried out	USA and Australia
Study type	Retrospective cohort study
Aim of the study	To determine whether reticular pseudodrusen (RPD) confer an increased risk of progression to late-stage age-related macular degeneration (AMD) in fellow eyes of those recently diagnosed with unilateral choroidal neovascularization (CNV).
Study dates	Published 2014 Participants recruited from 2010 to 2012
Source of funding	This work was in part supported by the German Research Council, the Perpetual Foundation, Novartis Australia, Bayer Australia, and by the National Health and Medical Research Council (NHMRC) project grants and Centre for Clinical Research Excellence grant, a Macular Degeneration Foundation Australia Research Grant (RHG & GSH), the BrightFocus Foundation, a National Institutes of Health grant, the American Macular Degeneration Foundation, Inc., the Helen K. and Arthur E. Johnson Foundation, the Willard L. Eccles Charitable Foundation, Sylvia E. Prahl-Brodbeck, Sharon E. Steele-McGee and an unrestricted grant to the University of Utah John A. Moran Eye Center and Department of Ophthalmology and Visual Sciences from Research to Prevent Blindness, Inc. CERA receives Operational Infrastructure Support from the Victorian Government.
Number of patients	200 consecutive participants with CNV secondary to AMD in one eye and no signs of late stage AMD in the fellow eye.
Inclusion Criteria	• Participants were recruited from the medical retina clinic at the Royal Victorian Eye and Ear Hospital at the University of Melbourne, Australia, and the John A. Moran Eye Center at the University of Utah, USA from 2010 until 2012. • All consecutive subjects who presented with a newly diagnosed CNV secondary to AMD were recruited. • Data was retrospectively reviewed to address the question of the fellow eye by including only those participants with non late-stage AMD in their fellow eye and follow-up for at least one year, unless they developed late-stage AMD in the fellow eye in less than one year, in which case they were not excluded from analyses.
Exclusion Criteria	• Exclusion criteria, for all participants, based upon the assessment of all images, included the presence of late-stage AMD (including any geographic atrophy (GA) and CNV) or other retinal pathology such as diabetic retinopathy or significant epiretinal membrane in the fellow study eye, and any corneal or media opacity that obscured the macula and prevented the assessment of disease state.

Bibliographic reference	**Finger,Robert P., Wu,Zhichao, Luu,Chi D., Kearney,Frances, Ayton,Lauren N., Lucci,Lucia M., Hubbard,William C., Hageman,Jill L., Hageman,Gregory S., Guymer,Robyn H., Reticular pseudodrusen: a risk factor for geographic atrophy in fellow eyes of individuals with unilateral choroidal neovascularization, Ophthalmology, 121, 1252-1256, 2014**
	• Participants had to have all required imaging, i.e. SD-OCT, NIR and colour fundus photography.
Diagnostic criteria	All participants underwent imaging with colour fundus photography, NIR and a 20°×20° volume scan with at least 19 B-scans on SD-OCT. Fluorescein angiography (FA) was performed at baseline presentation, and indocyanine green angiography (ICGA) and fundus autofluorescence (FAF) were performed as clinically indicated. End-stage disease was classified as either GA or CNV depending on whichever late stage was developed first. CNV was defined based on clinical examination and confirmed by SD-OCT and FA. GA was defined based on clinical examination and colour photography with lesions larger than 175 µm and within two disc diameters of the fovea and confirmed on SD-OCT and NIR. The presence of RPD was defined as groups of hypo-reflective lesions against a background of mild hyper-reflectance on NIR with corresponding hyper-reflective signal above the retinal pigment epithelium (RPE) on SD-OCT.
Patient characteristics	Participants (n=200) Age (years): 76.77 ±7.10 Gender Male: 79(39.5%) Female: 121(60.5%) Ethnicity: not reported
Predictors/risk factors and effect estimates	Risk factors of interest include: Retinal pseudodrusen, pigmentary changes, drusen ≥125 µm Hazard ratios were adjusted for the above factors and age and gender.
Outcomes	Hazard ratios for late-stage AMD Hazard rates for choroidal neovascularisation Hazard rates for geographic atrophy
Analysis used	Cox regression analysis

Bibliographic reference	**Finger,Robert P., Wu,Zhichao, Luu,Chi D., Kearney,Frances, Ayton,Lauren N., Lucci,Lucia M., Hubbard,William C., Hageman,Jill L., Hageman,Gregory S., Guymer,Robyn H., Reticular pseudodrusen: a risk factor for geographic atrophy in fellow eyes of individuals with unilateral choroidal neovascularization, Ophthalmology, 121, 1252-1256, 2014**
Length of follow up	All participants were followed up for an average of two years (±1.3 years standard deviation, median 2 years, range 7.4 years).
Missing data handling/loss to follow up	Participants had to have all required imaging to be included (no loss to follow up or missing data described)
Results	Results for hazard rates of late-stage AMD, controlling for age and gender **Choroidal neovascularisation (CNV)** Reticular pseudodrusen: 1.19 (0.72-1.94) Drusen ≥125µm: 1.96 (1.14-3.36) Pigmentary Changes: 2.49 (1.51-4.10) **Geographic atrophy (GA)** Reticular pseudodrusen: 4.93 (1.06-22.93) Drusen ≥125µm: 11.73 (1.47-93.81) Pigmentary Changes: 5.75 (2.09-15.84) **CNV or GA** Reticular pseudodrusen: 1.20 (0.76-1.89) Drusen ≥125µm: 2.08 (1.25-3.49) Pigmentary Changes: 2.55 (1.64-3.96)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE

Bibliographic reference	**Finger,Robert P., Wu,Zhichao, Luu,Chi D., Kearney,Frances, Ayton,Lauren N., Lucci,Lucia M., Hubbard,William C., Hageman,Jill L., Hageman,Gregory S., Guymer,Robyn H., Reticular pseudodrusen: a risk factor for geographic atrophy in fellow eyes of individuals with unilateral choroidal neovascularization, Ophthalmology, 121, 1252-1256, 2014**
	Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). UNSURE The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Grunwald,Juan E., Daniel,Ebenezer, Huang,Jiayan, Ying,Gui Shuang, Maguire,Maureen G., Toth,Cynthia A., Jaffe,Glenn J., Fine,Stuart L., Blodi,Barbara, Klein,Michael L., Martin,Alison A., Hagstrom,Stephanie A., Martin,Daniel F., CATT Research Group, Risk of geographic atrophy in the comparison of age-related macular degeneration treatments trials, Ophthalmology, 121, 150-161, 2014**
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To describe risk factors for geographic atrophy (GA) in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT).
Study dates	July 2010 and September 2011

Bibliographic reference	**Grunwald,Juan E., Daniel,Ebenezer, Huang,Jiayan, Ying,Gui Shuang, Maguire,Maureen G., Toth,Cynthia A., Jaffe,Glenn J., Fine,Stuart L., Blodi,Barbara, Klein,Michael L., Martin,Alison A., Hagstrom,Stephanie A., Martin,Daniel F., CATT Research Group, Risk of geographic atrophy in the comparison of age-related macular degeneration treatments trials, Ophthalmology, 121, 150-161, 2014**
Source of funding	Supported by cooperative agreements from the National Eye Institute, National Institutes of Health, Department of Health and Human Services.
Number of patients	1024 patients were analysed
Inclusion Criteria	• Age ≥50 years • Active, untreated CNV secondary to AMD • VA between 20/25 and 20/320 in the study eye
Exclusion Criteria	• Eyes with any GA at baseline • Missing or ungradable fundus photography
Diagnostic criteria	At enrolment, patients provided a medical history and had bilateral colour fundus photography (CFP), fluorescein angiography (FA), and time-domain optical coherence tomography (OCT). Follow-up examinations were scheduled every 28 days for 2 years. Graders at the Photograph Reading Centre were required to indicate whether there were signs of GA at the initial visit in the study eye as well as the fellow eye. Two trained and certified graders at the CATT Fundus Photograph Reading Centre reviewed images acquired at the initial and follow-up visits. Discrepancies between the 2 graders were adjudicated. The diagnosis of GA required the presence within the macular vascular arcades of ≥1 patches ≥250 μ in longest linear dimension of partial or complete depigmentation in the CFP that had ≥1 of these additional characteristics: sharply demarcated borders seen in CFP and/or FA, visibility of underlying choroidal vessels, excavated or punched out appearance on stereoscopy of CFP or FA, or uniform hyperfluorescence bounded by sharp borders on late-phase angiography. OCT scans were not used for the determination of the presence of GA.
Patient characteristics	Total (n=1024) Age (yrs), No. 50–69: 128 70–79: 354

Bibliographic reference	**Grunwald,Juan E., Daniel,Ebenezer, Huang,Jiayan, Ying,Gui Shuang, Maguire,Maureen G., Toth,Cynthia A., Jaffe,Glenn J., Fine,Stuart L., Blodi,Barbara, Klein,Michael L., Martin,Alison A., Hagstrom,Stephanie A., Martin,Daniel F., CATT Research Group, Risk of geographic atrophy in the comparison of age-related macular degeneration treatments trials, Ophthalmology, 121, 150-161, 2014**
	80–89: 476 ≥90: 66 Sex, No. Female 634 Male 390 Ethnicity (not reported)
Predictors/risk factors and effect estimates	Risk factors of interest for which hazard ratios were provided included: Baseline VA in study eye, retinal angiomatous proliferation lesion, geographic atrophy in fellow eye Covariates and risk factors at the univariate level included: age, baseline VA of the study eye, baseline VA of fellow eye, location of lesion, lesion type, blocked fluorescence, RAP lesion, CNV in fellow eye, GA in fellow eye, retinal thickness in the foveal centre, subretinal thickness in the foveal centre, subretinal tissue complex thickness in the foveal centre, intraretinal fluid, subretinal fluid, vitreomacular attachment, drug, and regimen, atrophic or fibrotic scar, gender, cigarette smoking, hypertension, diabetes, dietary supplement use, hypercholesterolemia
Outcomes	Multivariate Analysis and hazard ratios for factors Associated with Incidence of Geographic Atrophy (GA) at 2 Years
Analysis used	Cox proportional hazard models
Length of follow up	2 years
Missing data handling/loss to follow up	Those with missing data were excluded (for instance missing information on presence of geographic atrophy). No imputations were made
Results	Multivariate Analysis for Factors Associated with Incidence of Geographic Atrophy (GA) at 2 Years Baseline VA in study eye 20/25–40: 1.00 (referent) 20/50–80: 1.66 (1.14–2.44) 20/100–160: 1.70 (1.10–2.62) 20/200–320: 2.65 (1.43–4.93)

Bibliographic reference	**Grunwald,Juan E., Daniel,Ebenezer, Huang,Jiayan, Ying,Gui Shuang, Maguire,Maureen G., Toth,Cynthia A., Jaffe,Glenn J., Fine,Stuart L., Blodi,Barbara, Klein,Michael L., Martin,Alison A., Hagstrom,Stephanie A., Martin,Daniel F., CATT Research Group, Risk of geographic atrophy in the comparison of age-related macular degeneration treatments trials, Ophthalmology, 121, 150-161, 2014**
	Retinal angiomatous proliferation lesion No: 1.00 (referent) Yes: 1.69 (1.16–2.47) GA in fellow eye None/questionable: 1.00 (referent) Present: 2.07 (1.40–3.08) Initial model includes age, baseline VA of the study eye, baseline VA of fellow eye, location of lesion, lesion type, blocked fluorescence, RAP lesion, CNV in fellow eye, GA in fellow eye, retinal thickness in the foveal centre, subretinal thickness in the foveal centre, subretinal tissue complex thickness in the foveal centre, intraretinal fluid, subretinal fluid, vitreomacular attachment, drug, and regimen. The final multivariate model only included the significant variables listed in this table. Risk factors found non-significant at univariate level included: atrophic or fibrotic scar, gender, cigarette smoking, hypertension, diabetes, dietary supplement use, hypercholesterolemia
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). PARTLY

Bibliographic reference	**Grunwald,Juan E., Daniel,Ebenezer, Huang,Jiayan, Ying,Gui Shuang, Maguire,Maureen G., Toth,Cynthia A., Jaffe,Glenn J., Fine,Stuart L., Blodi,Barbara, Klein,Michael L., Martin,Alison A., Hagstrom,Stephanie A., Martin,Daniel F., CATT Research Group, Risk of geographic atrophy in the comparison of age-related macular degeneration treatments trials, Ophthalmology, 121, 150-161, 2014**
	Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Hahn,Paul, Acquah,Kofi, Cousins,Scott W., Lee,Paul P., Sloan,Frank A., Ten-year incidence of age-related macular degeneration according to diabetic retinopathy classification among medicare beneficiaries, Retina (Philadelphia, Pa.)Retina, 33, 911-919, 2013**
Country/ies where the study was carried out	USA
Study type	Longitudinal retrospective cohort analysis
Aim of the study	To compare the longitudinal incidence over 10 years of dry and wet age-related macular degeneration (AMD) in a U.S. sample of Medicare beneficiaries with: no diabetes mellitus (no DM); diabetes mellitus without retinopathy (DM); non-proliferative diabetic retinopathy (NPDR); and proliferative diabetic retinopathy (PDR).
Study dates	Published 2013 Patients enrolled between 1995-2005
Source of funding	Publication of this article was supported in part by a grant from the National Institute on Aging. Paul Hahn received support from the Ronald G. Michels Foundation and the Heed Ophthalmic Foundation. Paul P. Lee has served as a consultant for

Bibliographic reference	**Hahn,Paul, Acquah,Kofi, Cousins,Scott W., Lee,Paul P., Sloan,Frank A., Ten-year incidence of age-related macular degeneration according to diabetic retinopathy classification among medicare beneficiaries, Retina (Philadelphia, Pa.)Retina, 33, 911-919, 2013**
	Allergan, Pfizer, and Genentech, and he has received financial support from Alcon, the National Institute of Health, and the Washington University Award
Number of patients	Diabetes mellitus (n=6621) Non-proliferative diabetic retinopathy (n=1307) Proliferative diabetic retinopathy (n=327) Compared to an equivalent number of controls without diabetes
Inclusion Criteria	• A sample of individuals first diagnosed with DM, NPDR, or PDR in 1995. • Individuals with a new diagnosis of PDR required exclusion of any previous PDR code in the prior 4 years. • Individuals with a new diagnosis of NPDR required exclusion of any previous NPDR or PDR diagnosis in the prior 4 years. • Individuals with a new diagnosis of DM required exclusion of any previous DM, NPDR, or PDR diagnosis in the prior 4 years.
Exclusion Criteria	• Individuals age 95+ in 1995 and persons who entered a Medicare risk plan (HMO) or • Lived outside of the U.S for 12 months or more during the look-back period. • Any individual initially diagnosed with AMD prior to a diabetes mellitus or diabetic retinopathy diagnosis in 1995. • Any individual who had not seen an eye care provider at least once during the look-back and at least once during both the first and the last five years of the follow-up period.
Diagnostic criteria	Under a Duke University Institutional Review Board-approved protocol, Medicare 5% inpatient, outpatient, and Part B claims files were used to identify a nationally representative sample of Medicare beneficiaries aged 65 or older who were diagnosed with DM, NPDR, and PDR or dry AMD and wet AMD from 1991–2005. Diagnosis was based on ICD-9-CM codes for the appropriate disease state (Table 1). Individuals with no DM were identified by exclusion of all diabetes mellitus codes; individuals with no AMD were identified by exclusion of all AMD codes. To ensure these were incident cases of diabetes mellitus or diabetic retinopathy and to identify other comorbidities, authors employed a 4-year look-back period, which necessitated all individuals to be age 69+ in 1995 in order to have a full look-back. Individuals with a new diagnosis of PDR required exclusion of any previous PDR code in the look-back; individuals with a new diagnosis of NPDR required exclusion of any previous NPDR or PDR diagnosis in the look-back;

Bibliographic reference	**Hahn,Paul, Acquah,Kofi, Cousins,Scott W., Lee,Paul P., Sloan,Frank A., Ten-year incidence of age-related macular degeneration according to diabetic retinopathy classification among medicare beneficiaries, Retina (Philadelphia, Pa.)Retina, 33, 911-919, 2013**
	individuals with a new diagnosis of DM required exclusion of any previous DM, NPDR, or PDR diagnosis in the look-back period.
Patient characteristics	Individuals with DM, NPDR, and PDR were matched at baseline to an equivalent number of 'no DM' controls by age, gender, race, history of hypertension, atherosclerosis, stroke, coronary heart disease, hyperlipidaemia, and Charlson index. All variables were matched between diabetic/diabetic retinopathy subtypes and controls except for the Charlson index, which could not be matched to a standard difference <10% for individuals with NPDR or PDR.
Predictors/risk factors and effect estimates	Risk factors under study included: Diabetes, diabetic proliferative retinopathy and diabetic non-proliferative retinopathy
Outcomes	Hazard Ratio (95% CI) for Development of Dry AMD Hazard Ratio (95% CI) for Development of Wet AMD
Analysis used	Cox proportional hazard modelling
Length of follow up	10 year follow up
Missing data handling/loss to follow up	The Medicare database represents information collected for billing purposes and not for the analysis of clinical investigations. Relevant conditions may sometimes have been incorrectly coded. The database includes clinically ambiguous codes, including 362.81 (retinal haemorrhage: preretinal, retinal (deep) (superficial), subretinal), which may arise secondary to either non-proliferative or proliferative/neovascular aetiologies or 362.57 (drusen), which is often used to code for peripheral drusen not diagnostic for macular degeneration. While they did not include these ambiguous codes in our final analysis, a parallel analysis was performed with inclusion of these codes (data not shown), resulting in similar results with significantly increased risk of wet AMD (but not dry AMD) in patients with NPDR and PDR only.
Results	**Hazard Ratio (95% CI) for Development of Dry AMD** Diabetes mellitus 1.03 (0.97 1.09) Non-proliferative diabetic retinopathy 1.24 (1.08 1.43) Proliferative diabetic retinopathy 1.10 (0.83 1.47) **Hazard Ratio (95% CI) for Development of Wet AMD**

Bibliographic reference	**Hahn,Paul, Acquah,Kofi, Cousins,Scott W., Lee,Paul P., Sloan,Frank A., Ten-year incidence of age-related macular degeneration according to diabetic retinopathy classification among medicare beneficiaries, Retina (Philadelphia, Pa.)Retina, 33, 911-919, 2013**
	Diabetes mellitus 1.11 (0.97 1.27) Non-proliferative diabetic retinopathy 1.68 (1.23 2.31) Proliferative diabetic retinopathy 2.15 (1.07 4.33) Controlled for other variables in the Cox proportional analysis including systemic comorbidities and the Charlson index
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). YES Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). NO Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Howard,Kerri P., Klein,Barbara E.K., Lee,Kristine E., Klein,Ronald, Measures of body shape and adiposity as related to incidence of age-related eye diseases: observations from the Beaver Dam Eye Study, Investigative ophthalmology & visual science, 55, 2592-2598, 2014**
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To examine the effect of obesity on the incidence of age-related eye disease.
Study dates	Published 2014 1988-1990 through 2008-2010
Source of funding	Supported by National Institutes of Health Grant. The National Eye Institute provided funding for entire study, including collection and analyses of data. Additional support was provided by an unrestricted grant from Research to Prevent Blindness.
Number of patients	2641 participants (870 female non-smokers, 640 female smokers, 368 male non-smokers, and 763 male smokers contributing 1824, 1334, 803, and 1606 person-visits, respectively)
Inclusion Criteria	A private census of the population of Beaver Dam, Wisconsin All residents aged 43- 84 years To contribute to analysis in a given 5-year interval, a person must have had complete data on the risk factors of interest (BMI, WHR, WC, or WHtR) and the outcome (incident nuclear, cataract, cortical cataract, or PSC, cataract surgery, or early or late AMD) and all covariates included in the maximally adjusted model (age, sedentary lifestyle, diabetes, hypertension).
Exclusion Criteria	None described
Diagnostic criteria	Photographs of the retina were taken to determine presence and severity of lesions associated with AMD and the Wisconsin Age-related Maculopathy Grading System was used to assess the fundus photographs. Early AMD was defined by the presence of soft indistinct drusen or any type of drusen associated with pigmentary abnormality (i.e., retinal pigment epithelium depigmentation or increased retinal pigment). Late AMD was defined by the presence of neovascular macular degeneration or pure geographic atrophy (GA).
Patient characteristics	Original sample Age at baseline (n=4755) 43- 54: 1500

Bibliographic reference	Howard,Kerri P., Klein,Barbara E.K., Lee,Kristine E., Klein,Ronald, Measures of body shape and adiposity as related to incidence of age-related eye diseases: observations from the Beaver Dam Eye Study, Investigative ophthalmology & visual science, 55, 2592-2598, 2014
	55-64: 1295 65-74: 1242 75-86: 718 Gender (n): Women: 2642 Men: 2113 Ethnicity: 99% white
Predictors/risk factors and effect estimates	Risk factors of interest under study included: Gender, smoking, BMI Outcomes were adjusted for: age (age and age squared for cataract outcomes), sedentary lifestyle, hypertension, diabetes, posterior subscapular cataract.
Outcomes	Hazard ratios for the risk of developing early AMD stratified by gender (and smoking status) Hazard ratios for the risk of developing late AMD stratified by gender (and smoking status)
Analysis used	Discrete-time hazard model with complementary log-log link function and time varying predictors
Length of follow up	15 years
Missing data handling/loss to follow up	Generally, persons who were excluded from analysis were older and had more comorbid conditions compared with those included. For those included, female smokers tended to be younger than non-smokers. There were no significant differences between female non-smokers and smokers with respect to systolic or diastolic blood pressure, education level, BMI, WC, WHR, WHtR, heavy drinking, cardiovascular disease, hypertension, diabetes, having a sedentary lifestyle, or using vitamins. In males, non-smokers tended to be older and have more years of education and smaller WC as compared with male smokers. Male smokers were more likely to have ever been a heavy drinker, have cardiovascular disease, or diabetes and were less likely to have a sedentary lifestyle. No description of how missing data or loss to follow up was dealt, with as participants were not included in the analysis unless they had complete information.

Bibliographic reference	Howard,Kerri P., Klein,Barbara E.K., Lee,Kristine E., Klein,Ronald, Measures of body shape and adiposity as related to incidence of age-related eye diseases: observations from the Beaver Dam Eye Study, Investigative ophthalmology & visual science, 55, 2592-2598, 2014
Results	**Hazard ratios for the risk of developing early AMD stratified by gender (and smoking status)** Female, non-smoker: BMI (per 2.5 kg/m²): 1.10 (1.02, 1.19) Male, non-smoker: BMI (per 2.5 kg/m²): 0.90 (0.75, 1.07) **Hazard ratios for the risk of developing late AMD stratified by gender (and smoking status)** Female, non-smoker BMI (per 2.5 kg/m²): 1.31 (1.15, 1.50) Male, non-smoker BMI (per 2.5 kg/m²): 0.86 (0.61, 1.20) **Hazard ratios for the risk of developing early AMD stratified by gender (and smoking status)** Female smoker BMI (per 2.5 kg/m²): 1.07 (0.98, 1.17) Male smoker BMI (per 2.5 kg/m²): 1.00 (0.90, 1.10) **Hazard ratios for the risk of developing late AMD stratified by gender (and smoking status)** Female smoker BMI (per 2.5 kg/m²): 0.99 (0.81, 1.21) Male smoker

Bibliographic reference	**Howard,Kerri P., Klein,Barbara E.K., Lee,Kristine E., Klein,Ronald, Measures of body shape and adiposity as related to incidence of age-related eye diseases: observations from the Beaver Dam Eye Study, Investigative ophthalmology & visual science, 55, 2592-2598, 2014**
	BMI (per 2.5 kg/m²): cannot estimate Hazard ratios adjusted for: age (age and age squared for cataract outcomes), sedentary lifestyle, hypertension, diabetes, posterior subscapular cataract.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). NO Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNCLEAR Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Klein,Barbara E.K., Howard,Kerri P., Gangnon,Ronald E., Dreyer,Jennifer O., Lee,Kristine E., Klein,Ronald, Long-term use of aspirin and age-related macular degeneration, JAMA, 308, 2469-2478, 2012
Country/ies where the study was carried out	USA
Study type	Longitudinal prospective cohort study
Aim of the study	To examine the association of regular aspirin use with incidence of AMD.
Study dates	Published 2012 1988–1990 through 2008–2010
Source of funding	This research is supported by National Institutes of Health grant EY06594. The National Eye Institute provided funding for entire study, including collection and analyses of data.
Number of patients	4926 person participated in the baseline examination
Inclusion Criteria	• To be eligible for incidence of a specified type of AMD (early, late, neovascular, pure GA) and inclusion in the analysis, a participant must • Be free of the given AMD outcome at the baseline examination and have complete AMD data from consecutive follow-up examinations, until incidence or censoring occurred. • A participant must have had complete data for self-reported aspirin use, age, sex, education, history of arthritis, and history of CVD.
Exclusion Criteria	• Participants with missing aspirin data were excluded
Diagnostic criteria	Participants were asked if they regularly used aspirin at least twice per week for more than 3 months. This self-report of regular aspirin use was the main exposure measure of interest in our primary analysis because it was asked at every examination. Additional information concerning frequency of aspirin use (<1 every other day, 1 every other day, 1/day, 2/day, 3–7/day or ≥8/day) and dosage were obtained at the third, fourth, and fifth examinations. Participants were asked to bring all currently used medications to the examinations. All medications, including NSAIDs and anticoagulants (e.g. warfarin), were recorded. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, and/or history of blood pressure medication use. Blood samples were obtained and analysed for glycosylated haemoglobin A1c and inflammatory factors, e.g. leukocyte count and C-reactive protein (CRP). CRP was measured only at the baseline examination, and leukocyte count was measured at the baseline and second examinations.

Bibliographic reference	Klein,Barbara E.K., Howard,Kerri P., Gangnon,Ronald E., Dreyer,Jennifer O., Lee,Kristine E., Klein,Ronald, Long-term use of aspirin and age-related macular degeneration, JAMA, 308, 2469-2478, 2012
	Diabetes was defined as self-report confirmed by use of insulin or diet to control diabetes, self-report with glycosylated haemoglobin A1c level above 6.5%, or no self-report with glycosylated haemoglobin A1c above 7%. Photographs of the retina were taken after pupillary dilation and graded in masked fashion by experienced graders using the Wisconsin Age-Related Maculopathy Grading System to assess the presence and severity of lesions associated with AMD.
Patient characteristics	Persons aged 43–86 years were included 99% was white 56% was female
Predictors/risk factors and effect estimates	Risk factors under study included aspirin use at the examination 5 years prior to incidence as well as aspirin use reported at the previous examination, 10 years prior to observed incidence. Variables potentially associated with risk of AMD were first analysed individually in age- and sex-adjusted models. These variables included body mass index, annual income, education, diabetes, systolic and diastolic blood pressure, hypertension, history of cancer, smoking (never, past, current), ever drinking, ever heavy drinking, history of arthritis, and history of CVD. All significant factors in the age- and sex-adjusted models were then included in a maximally adjusted model.
Outcomes	Hazard ratios for the development of early AMD, any late AMD, neovascular AMD or geographic atrophy.
Analysis used	Discrete-time hazard model using the complementary log-log link function with time-varying predictors
Length of follow up	20 year follow up. The mean duration of follow-up time was 14.8 years, with a median duration of 15.9 years
Missing data handling/loss to follow up	For incident early AMD, 2547 persons of the 4926 seen at baseline were excluded from analysis (1008 had prevalent early or late AMD at baseline, 84 persons were missing a covariate, 448 were missing AMD data at baseline, and 1007 did not have data at the first follow-up examination). For incidence of late AMD, 1794 persons of the 4926 seen at baseline were excluded from analysis (74 persons had prevalent late AMD at baseline, 104 were missing a covariate, 407 had missing AMD data at baseline, and 1209 had missing data at the first follow-up examination). Participants included in these analyses tended to be younger and have fewer comorbidities at baseline than those excluded.
Results	Relationships of Incidence of Age-related Macular Degeneration Outcomes with Self-Reported Regular Aspirin Use 5 Years Prior Over 20 Years in the Beaver Dam Eye Study. Hazard ratios (95% confidence intervals).

Bibliographic reference	Klein,Barbara E.K., Howard,Kerri P., Gangnon,Ronald E., Dreyer,Jennifer O., Lee,Kristine E., Klein,Ronald, Long-term use of aspirin and age-related macular degeneration, JAMA, 308, 2469-2478, 2012
	Early AMD* No regular aspirin use: Referent Regular aspirin use: 0.86 (0.71, 1.05) Any Late AMD No regular aspirin use: Referent Regular aspirin use: 1.21 (0.84, 1.74) Neovascular AMD No regular aspirin use: Referent Regular aspirin use: 1.07 (0.68, 1.67) Pure GA No regular aspirin use: Referent Regular aspirin use: 1.65 (0.91, 2.99) Hazard ratios were adjusted for age, arthritis history, and education level
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). YES Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). YES

Bibliographic reference	Klein,Barbara E.K., Howard,Kerri P., Gangnon,Ronald E., Dreyer,Jennifer O., Lee,Kristine E., Klein,Ronald, Long-term use of aspirin and age-related macular degeneration, JAMA, 308, 2469-2478, 2012
	Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Klein,Michael L., Francis,Peter J., Ferris,Frederick L., Hamon,Sara C., Clemons,Traci E., Risk assessment model for development of advanced age-related macular degeneration, Archives of ophthalmology, 129, 1543-1550, 2011
Country/ies where the study was carried out	USA
Study type	Prospective Cohort Study
Aim of the study	To design a risk assessment model for development of advanced age-related macular degeneration (AMD) incorporating phenotypic, demographic, environmental, and genetic risk factors.
Study dates	Published 2011 Participants in the Age-Related Eye Disease Study
Source of funding	This work was supported by the Casey Eye Institute Macular Degeneration Fund, Research to Prevent Blindness, the Bea Arveson Macular Degeneration Fund, and the Foundation Fighting Blindness.
Number of patients	2846 participants
Inclusion Criteria	• Age 55-80 years

Bibliographic reference	Klein,Michael L., Francis,Peter J., Ferris,Frederick L., Hamon,Sara C., Clemons,Traci E., Risk assessment model for development of advanced age-related macular degeneration, Archives of ophthalmology, 129, 1543-1550, 2011
	• At least one eye had to be free from vision-threatening disease other than AMD and cataract • That eye could not have had surgery, except for cataract surgery • The participants' stages of disease ranged from no evidence of AMD in either eye, to advanced AMD with vision loss in one eye but good vision (at least 20/30) in the other eye
Exclusion Criteria	None described
Diagnostic criteria	Comprehensive ocular and medical histories and examinations were performed at entrance into the study. Recorded information included age, sex, race, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), education level, cigarette smoking, diet, sunlight exposure, history of skin cancer, arthritis, systemic hypertension, other cardiovascular diseases, diabetes, and history of current and past medications and dietary supplements. For this study, the AREDS simplified severity scale was used to classify participants by their retina phenotype; This scale was designed to define risk categories for development of advanced AMD that could be readily determined by either clinical examination or fundus photography. The system uses 2 retinal abnormalities at baseline to determine a risk score: The end points of this study occurred when participants with no advanced AMD in either eye at baseline progressed to advanced AMD in either eye or when those with advanced AMD in 1 eye at baseline developed advanced AMD in the fellow eye. Two forms of advanced AMD were recognized: (1) NV and (2) GA, defined as an area of well-demarcated depigmentation of the pigment epithelium, typically round or oval, and within which choroidal vessels are usually visible.
Patient characteristics	Median Age: 69 years 56% female Only white ethnicity included in the analysis
Predictors/risk factors and effect estimates	Risk factors of interest were: Very large drusen, Current smoking, Family history, AAMD in 1 eye, Age, mean (SD), y Hazard ratios were adjusted for age, cigarette smoking, family history, BMI, education, simple scale score, very large drusen (250 µm), unilateral AMD, and variants in the genes CFH, ARMS2, C3, and CFI. The C2/CFB variant. (all significant at univariate level)
Outcomes	Hazard Ratios for Progression to Advanced Age-Related Macular Degeneration

Bibliographic reference	Klein,Michael L., Francis,Peter J., Ferris,Frederick L., Hamon,Sara C., Clemons,Traci E., Risk assessment model for development of advanced age-related macular degeneration, Archives of ophthalmology, 129, 1543-1550, 2011
Analysis used	Cox proportional hazards analysis
Length of follow up	Follow-up averaged 9.3 years
Missing data handling/loss to follow up	Unclear: no description of missing data or how this was managed.
Results	Multivariate Association of Baseline Independent Variables Included in Final Model With Hazard Ratios for Progression to Advanced Age-Related Macular Degeneration at 2, 5, and 10 Years in 2602 Participants Very large drusen No: 1 (referent) Yes: 1.79 (1.50-2.14) Current smoking No: 1 (referent) Yes: 1.78 (1.37-2.31) Family history No: 1 (referent) Yes: 1.40 (1.16-1.70) AAMD in 1 eye No: 1 (referent) Yes 1.21 (1.02-1.45) Age, mean (SD), y: 1.03 (1.01-1.05) Education and BMI were not significant at the multivariate level.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in Studies of prognostic factors

Bibliographic reference	Klein,Michael L., Francis,Peter J., Ferris,Frederick L., Hamon,Sara C., Clemons,Traci E., Risk assessment model for development of advanced age-related macular degeneration, Archives of ophthalmology, 129, 1543-1550, 2011
	Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). PARTLY Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Klein,R., Klein,B.E., Knudtson,M.D., Meuer,S.M., Swift,M., Gangnon,R.E., 20070220, Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, Ophthalmology, 114, 253-262, 2007
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To describe the 15-year cumulative incidence of signs of early and late age-related macular degeneration (AMD)

Bibliographic reference	Klein,R., Klein,B.E., Knudtson,M.D., Meuer,S.M., Swift,M., Gangnon,R.E., 20070220, Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, Ophthalmology, 114, 253-262, 2007
Study dates	1988-1990 to 1993-1995 follow up and/or 2003-2005 follow up.
Source of funding	Supported by National Institutes of Health, National Eye institute, and, in part, Research to Prevent Blindness.
Number of patients	Included 3917 persons
Inclusion Criteria	A private census of the population of Beaver Dam, Wisconsin All residents aged 43- 84 years
Exclusion Criteria	None reported
Diagnostic criteria	Similar procedures were performed at baseline and follow up examinations. Stereoscopic 30° colour fundus photographs were taken, focused on the disc and macula and a non-stereoscopic colour fundus photograph temporal to but including the fovea of each eye. A circular grid was placed on one photographic slide of the stereoscopic pair, which divided the macular area into nine subfields, consisting of a central circle (a single subfield), inner ring (comprised of the four inner subfields), and outer ring (comprised of four outer subfields). Circles of defined size printed on clear acetate were used to estimate size of drusen and areas involved by drusen, increased retinal pigment and retinal pigment epithelial (RPE) depigmentation. Two gradings were performed for each eye at examination. First, a preliminary masked grading was done by one of two senior graders. Next, detailed gradings were performed by one of three other experienced graders. Each eye was graded independently of the fellow eye. The assessment consisted of a subfield-by-subfield, lesionby-lesion, evaluation of each photograph set using the Wisconsin Age-Related Maculopathy Grading System. Increasing order of severity of drusen were defined as follows: hard distinct, soft distinct, and soft indistinct. The incidence of a specific lesion, e.g., reticular drusen, geographic atrophy (GA), or exudative AMD, was defined by its presence at follow-up when it was not present at baseline. The incidence of late AMD was defined by the appearance of either exudative macular degeneration or pure GA at follow-up when neither lesion was present at baseline. Incidence of early AMD was defined by either the presence of either soft indistinct drusen or RPE depigmentation, or increased retinal pigment together with any type of drusen at follow-up when none of these lesions was present at baseline. Incidence of late AMD was defined by the appearance of either exudative macular degeneration or pure geographic atrophy at follow up when neither lesion was present at baseline.
Patient characteristics	Age at baseline 43- 54: 58% 55-64: 26%

Bibliographic reference	Klein,R., Klein,B.E., Knudtson,M.D., Meuer,S.M., Swift,M., Gangnon,R.E., 20070220, Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, Ophthalmology, 114, 253-262, 2007
	65-74: 26% 75-86: 16% Gender (n): Women: 2642 Men: 2113 Ethnicity: 99% white
Predictors/risk factors and effect estimates	Risk factors of interest under study included: Age (by increasing categories, 43-54 years, 55-64 years, 65-74 years, 75-86 years); Drusen > 125µm vs <63µm in diameter; Soft distinct drusen vs hard distinct drusen; Soft indistinct vs soft distinct drusen or hard distinct drusen; Drusen area >16877 µm² vs ≤2596 µm²; Pigmentary abnormalities present vs absent; Increased pigment present vs absent; RPE depigmentation present vs absent. Odds ratios were adjusted by age (by increasing categories, 43-54 years, 55-64 years, 65-74 years, 75-86 years).
Outcomes	Risk of developing early AMD, odds ratios (95% confidence intervals) Risk of developing late AMD, odds ratios (95% confidence intervals) Risk of developing geographic atrophy, odds ratios (95% confidence intervals) Risk of developing exudative AMD, odds ratios (95% confidence intervals):
Analysis used	Cox proportional hazards model
Length of follow up	15 year follow up
Missing data handling/loss to follow up	In general, persons who did not participate in the 15-year follow-up were older at baseline than those who did. After adjusting for age, persons who did not participate were more likely to have fewer years of education completed and higher systolic blood pressure than persons who participated.
Results	Fifteen-year cumulative incidence of Age-related macular degeneration (AMD) **Risk of developing early AMD, odds ratios (95% confidence intervals)** Age (by increasing categories, 43-54 years, 55-64 years, 65-74 years, 75-86 years): 2.3 (2.1-2.6)

Bibliographic reference	Klein,R., Klein,B.E., Knudtson,M.D., Meuer,S.M., Swift,M., Gangnon,R.E., 20070220, Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, Ophthalmology, 114, 253-262, 2007
	Drusen > 125µm vs <63µm in diameter: 5.5 (3.5-8.7) Soft distinct drusen vs hard distinct drusen: 3.0 (2.2-4.1) Drusen area >16877 µm² vs ≤2596 µm²: 5.2 (3.7-7.5) **Risk of developing late AMD, odds ratios (95% confidence intervals)** Age (by increasing categories, 43-54 years, 55-64 years, 65-74 years, 75-86 years): 3.5 (2.8- 4.4) Drusen > 125µm vs <63µm in diameter: 29.6 (14.4-60.7) Soft distinct drusen vs hard distinct drusen: 3.6 (1.5-8.6) Soft indistinct vs soft distinct drusen or hard distinct drusen: 17.5 (10.3-29.8) Drusen area >16877 µm² vs ≤2596 µm²: 32.3 (7.8-133) Pigmentary abnormalities present vs absent: 10.8 (6.5-18.0) Increased pigment present vs absent: 9.8 (5.9-16.3) RPE depigmentation present vs absent: 10.5 (5.9-18.5) **Risk of developing exudative AMD, odds ratios (95% confidence intervals)** Age (by increasing categories, 43-54 years, 55-64 years, 65-74 years, 75-86 years): 2.9 (2.2-3.8) Drusen > 125µm vs <63µm in diameter: 60.4 (17.7-206) Soft distinct drusen vs hard distinct drusen: 7.4 (2.4-22.6) Soft indistinct vs soft distinct drusen or hard distinct drusen: 18.3 (8.9-37.4) Drusen area >16877 µm² vs ≤2596 µm²: 40.4 (5.5-297) Pigmentary abnormalities present vs absent: 7.2 (3.6-14.1) Increased pigment present vs absent: 5.8 (2.9-11.7) RPE depigmentation present vs absent: 7.8 (3.6-16.6) **Risk of developing geographic atrophy, odds ratios (95% confidence intervals)** Age (by increasing categories, 43-54 years, 55-64 years, 65-74 years, 75-86 years): 4.2 (2.9-6.1)

Bibliographic reference	Klein,R., Klein,B.E., Knudtson,M.D., Meuer,S.M., Swift,M., Gangnon,R.E., 20070220, Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, Ophthalmology, 114, 253-262, 2007
	Drusen > 125µm vs <63µm in diameter: 14.5 (5.9-35.7) Soft distinct drusen vs hard distinct drusen: 1.2 (0.3-5.7) Soft indistinct vs soft distinct drusen or hard distinct drusen: 14.6 (6.8-31.1) Drusen area >16877 µm² vs ≤2596 µm²: 24.0 (3.2-179) Pigmentary abnormalities present vs absent: 15.2 (7.3-31.6) Increased pigment present vs absent: 15.8 (7.6-32.8) RPE depigmentation present vs absent: 11.1 (5.0-24.4)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY

Bibliographic reference	Klein,R., Klein,B.E., Knudtson,M.D., Meuer,S.M., Swift,M., Gangnon,R.E., 20070220, Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, Ophthalmology, 114, 253-262, 2007
	The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Klein,R., Meuer,S.M., Knudtson,M.D., Iyengar,S.K., Klein,B.E., 20080320, The epidemiology of retinal reticular drusen, American journal of ophthalmology, 145, 317-326, 2008
Country/ies where the study was carried out	Beaver Dam, USA
Study type	Prospective cohort study
Aim of the study	To document the long term incidence of reticular drusen, its risk factors and association with a high risk of incident late AMD.
Study dates	From fall 1987 to April 30, 2005
Source of funding	The National Eye Institute provided funding for entire study including collection and analyses and of data
Number of patients	4,926 persons 3,684 participated in 5 year follow up 2,764 participated in 10 year follow up 2,119 participated in 15 year follow up examinations
Inclusion Criteria	A private census of the population of Beaver Dam, Wisconsin All residents aged 43- 84 years
Exclusion Criteria	None reported
Diagnostic criteria	In brief, a circular grid was placed on one photographic slide of the stereoscopic pair, which divided the macular area into nine subfields, consisting of a central circle (a single subfield), inner ring (comprised of the four inner subfields), and outer ring (comprised of four outer subfields). Reticular and other types of drusen were graded in each subfield, outside the grid in DRS field 2, and nasal to the disc in Field 1. Two gradings were performed for each eye at each examination. First, a preliminary masked grading was done by one of two senior graders. Next, detailed gradings were performed by one of three other experienced graders. Each eye was graded independently of the fellow eye. The assessment consisted of a

Bibliographic reference	Klein,R., Meuer,S.M., Knudtson,M.D., Iyengar,S.K., Klein,B.E., 20080320, The epidemiology of retinal reticular drusen, American journal of ophthalmology, 145, 317-326, 2008
	subfield-by-subfield, lesionby-lesion, evaluation of each photograph set using the Wisconsin Age-Related Maculopathy Grading System. Increasing order of severity of drusen were defined as follows: hard distinct, soft distinct, and soft indistinct. The incidence of a specific lesion, e.g., reticular drusen, geographic atrophy (GA), or exudative AMD, was defined by its presence at follow-up when it was not present at baseline. The incidence of late AMD was defined by the appearance of either exudative macular degeneration or pure GA at follow-up when neither lesion was present at baseline.
Patient characteristics	Age at baseline (n=4755) 43- 54: 1500 55-64: 1295 65-74: 1242 75-86: 718 Gender (n): Women: 2642 Men: 2113 Ethnicity: 99% white
Predictors/risk factors and effect estimates	Controlling for gender (male/female), education (<high school, high school, some college, higher than college), income (<10K, 10-19K, 20-29K, 30-44K, 45 plus), smoking history (never/past/current), history of current wine drank (none, 1 per week, 2 plus per week), History of current liquor drank (none, 1 per week, 2-3 per week, 4 plus per week), history of sunlight at work (<25%, 25%, >25%), History of UV protection (none, little moderate, high) Diabetes, History of average distance walk/day (none, 1-4 blocks, 5-12 blocks, 13 plus blocks), History of sedentary lifestyle, history of antidepressant use.
Outcomes	Multivariable model of relationships of characteristics to incident reticular drusen, and relationship of reticular drusen at baseline to the 15-year cumulative incidence of late AMD, Geographic atrophy and exudative AMD
Analysis used	Age-adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated from discrete logistic hazard regression models for incidence.
Length of follow up	15 years

Bibliographic reference	Klein,R., Meuer,S.M., Knudtson,M.D., Iyengar,S.K., Klein,B.E., 20080320, The epidemiology of retinal reticular drusen, American journal of ophthalmology, 145, 317-326, 2008
Missing data handling/loss to follow up	In general, persons who did not participate in the 15-year follow-up were older at baseline than those who did. After adjusting for age, persons who did not participate were more likely to have fewer years of education completed and higher systolic blood pressure than persons who participated.
Results	Multivariable model of relationships of characteristics to incident reticular drusen in the Beaver Dam Eye study **Odds Ratio 95% (confidence interval)** Age 75-86 vs 43-54 years 47.3 (15.5, 144.3) 65-74 vs 43-54 years 22.9 (8.1, 65.3) 55-64 vs 43-54 years 5.8 (1.9, 17.3) Female sex 2.8 (1.6, 4.9) Increasing education 0.6 (0.4, 0.8) Smoking Current vs never smoker 1.9 (1.03, 3.6) Past vs never smoker 1.4 (0.9, 2.3) Increased wine drinking 0.6 (0.3, 1.1) Diabetes history 0.1 (0.02, 0.8) While controlling for age, history of pack-years smoked, current beer and heavy alcohol consumption, cumulative UV-exposure, hypertension status, weight, body mass, serum total and HDL cholesterol, cardiovascular disease history, iris colour, refractive error, cataract surgery, retinal pigmentary abnormalities were not related to the 15-year cumulative incidence of reticular drusen (data not shown). **Most Severe Drusen Type at Baseline OR (95% Confidence interval)** Risk of late AMD Reticular drusen vs Soft distinct drusen: 28.29 (9.48, 84.44) [reticular drusen higher risk] Reticular drusen vs Soft indistinct drusen: 6.34 (2.28, 17.63)

Bibliographic reference	Klein,R., Meuer,S.M., Knudtson,M.D., Iyengar,S.K., Klein,B.E., 20080320, The epidemiology of retinal reticular drusen, American journal of ophthalmology, 145, 317-326, 2008
	Risk of incident Geographic Atrophy Reticular drusen vs Soft distinct drusen: 41.78 (9.43,185.14) [reticular drusen higher risk] Reticular drusen vs Soft indistinct drusen: 6.23 (1.70, 22.73) Exudative AMD Reticular drusen vs Soft distinct drusen: 9.89 (2.16, 45.23) [reticular drusen higher risk] Reticular drusen vs Soft indistinct drusen: 2.82 (0.66, 12.01)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). PARTLY Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES

Bibliographic reference	Klein,R., Meuer,S.M., Knudtson,M.D., Iyengar,S.K., Klein,B.E., 20080320, The epidemiology of retinal reticular drusen, American journal of ophthalmology, 145, 317-326, 2008
	The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis) YES

Bibliographic reference	Klein,Ronald, Knudtson,Michael D., Cruickshanks,Karen J., Klein,Barbara E.K., Further observations on the association between smoking and the long-term incidence and progression of age-related macular degeneration: the Beaver Dam Eye Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 115-121, 2008
Country/ies where the study was carried out	Beaver Dam, USA
Study type	Longitudinal Cohort Study
Aim of the study	To describe the association between baseline smoking status, age at initiation, duration, intensity, pack-years, age at quitting, and time from the baseline examination since quitting and the 15-year cumulative incidence and progression of AMD.
Study dates	From fall 1987 to April 30, 2005
Source of funding	National Eye institute, National Institute of aging, Research to Prevent Blindness.
Number of patients	4,926 persons 3,684 participated in 5 year follow up 2,764 participated in 10 year follow up 2,119 participated in 15 year follow up examinations
Inclusion Criteria	A private census of the population of Beaver Dam, Wisconsin All residents aged 43- 84 year
Exclusion Criteria	Not specified
Diagnostic criteria	Informed consent was obtained from each participant at the beginning of the examination. Pertinent parts of the examinations included taking stereoscopic 30° colour fundus photographs cantered on the macula. The Wisconsin Age-Related Maculopathy Grading System was used to assess the presence and severity of lesions associated with AMD.

Bibliographic reference	**Klein,Ronald, Knudtson,Michael D., Cruickshanks,Karen J., Klein,Barbara E.K., Further observations on the association between smoking and the long-term incidence and progression of age-related macular degeneration: the Beaver Dam Eye Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 115-121, 2008**
	The incidence of early AMD was defined by the presence of soft, indistinct drusen or any type of drusen associated with RPE depigmentation or increased retinal pigment at follow-up when none of these lesions were seen at baseline. The incidence of exudative macular degeneration and pure geographic atrophy was defined by their presence at follow-up when neither was present at baseline. For each eye, a 6-level severity scale for AMD was defined as follows: Level 10. No drusen or hard drusen; or small soft drusen (125 µm in diameter) only, regardless of area of involvement, and no pigmentary abnormalities (increased retinal pigment or RPE depigmentation). Level 20. Hard drusen; or small soft drusen (125 µm in diameter), regardless of area of involvement, with increased retinal pigment but no RPE depigmentation; or soft drusen (125 µm in diameter) with a drusen area smaller than 196 350 µm2 (equivalent to a circle with a diameter of 500µm) and no pigmentary abnormalities. Level 30. Soft drusen (125 µm in diameter) with a drusen area smaller than 196 350 µm2 and RPE depigmentation; or soft drusen (125 µm in diameter) with an area 196 350 µm2 or larger with or without increased retinal pigment but no RPE depigmentation. Level 40. Soft drusen (125 µm in diameter) with a drusen area involvement 196 350 µm2 or larger and RPE depigmentation with or without increased retinal pigment. Level 50. Geographic atrophy in absence of exudative macular degeneration. Level 60. Exudative macular degeneration with or without geographic atrophy. Level 10 is equivalent to not having AMD; levels 20, 30, and 40 involve lesions that define early AMD of increasing severity (by type, size, area of drusen, and pigmentary abnormalities); while levels 50 and 60 involve lesions that define late AMD.
Patient characteristics	Age at baseline (n=4755) 43- 54: 1500 55-64: 1295 65-74: 1242 75-86: 718 Gender, no.:

Bibliographic reference	**Klein,Ronald, Knudtson,Michael D., Cruickshanks,Karen J., Klein,Barbara E.K., Further observations on the association between smoking and the long-term incidence and progression of age-related macular degeneration: the Beaver Dam Eye Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 115-121, 2008**
	Women: 2642 Men: 2113 Ethnicity: 99% white
Predictors/risk factors and effect estimates	Smoking variables under study: baseline smoking status, age at initiation, duration, intensity, pack-years, age at quitting, and time from the baseline examination since quitting. Controlling for age (categorically), sex (when appropriate) and baseline AMD severity level.
Outcomes	15 year cumulative incidence of Early AMD 15 year cumulative incidence of exudative AMD 15 year cumulative incidence of geographic atrophy
Analysis used	Multivariate odds ratios and 95% confidence intervals were calculated from discrete logistic hazard models.
Length of follow up	15 years
Missing data handling/loss to follow up	The analytical approach described above, allowed those who were right-censored (not seen after the 5- or 10-year examination owing to death or nonparticipation) to contribute information to the estimates. In general, persons who did not participate in the 15-year follow-up were older at baseline than those who did. After adjusting for age, persons who did not participate were more likely to have fewer years of education completed and higher systolic blood pressure than persons who participated.
Results	**15 year cumulative incidence of Early AMD** Adjusted odds ratios (95% confidence intervals) Past vs never smokers: 1.16 (0.91-1.48) Current vs never smokers:1.47 (1.08-1.99) Intensity, packs/d Ever smoked: 0.93 (0.75-1.15) Current smokers: 1.06 (0.65-1.73)

Bibliographic reference	Klein,Ronald, Knudtson,Michael D., Cruickshanks,Karen J., Klein,Barbara E.K., Further observations on the association between smoking and the long-term incidence and progression of age-related macular degeneration: the Beaver Dam Eye Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 115-121, 2008
	Duration, per 10 y Ever smoked: 1.02 (0.92-1.13) Current smokers: 0.98 (0.74-1.30) Pack-years, per 20 y Ever smoked: 1.02 (0.91-1.14) Current smokers: 1.08 (0.87-1.34) Age at initiation, per 10 y Ever smoked: 1.13 (0.97-1.31) Current smokers: 1.16 (0.88-1.52) Time since quitting, per 10 y Past smokers: 0.97 (0.83-1.13) Age at quitting, per 10 y Past smokers: 1.06 (0.91-1.23) **15 year cumulative incidence of Exudative AMD** Adjusted odds ratios (95% confidence intervals): Past vs never smokers: 1.12 (0.62-2.01) Current vs never smokers: 0.69 (0.27-1.76) Intensity, packs/d

Bibliographic reference	Klein,Ronald, Knudtson,Michael D., Cruickshanks,Karen J., Klein,Barbara E.K., Further observations on the association between smoking and the long-term incidence and progression of age-related macular degeneration: the Beaver Dam Eye Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 115-121, 2008
	Ever smoked: 0.94 (0.58-1.54) Current smokers: 1.12 (0.16-7.84) Duration, per 10 y Ever smoked: 1.16 (0.90-1.50) Current smokers: 0.76 (0.34-1.70) Pack-years, per 20 y Ever smoked 1.04 (0.83-1.31) Current smokers: 0.89 (0.37-2.14) Age at initiation, per 10 y Ever smoked: 1.03 (0.72-1.48) Current smokers: 1.42 (0.66-3.07) Time since quitting, per 10 y Past smokers: 0.78 (0.55-1.11) Age at quitting, per 10 y Past smokers: 1.38 (0.96-1.99) **15 year cumulative incidence of geographic atrophy** Adjusted odds ratios (95% confidence intervals): Past vs never smokers: 0.88 (0.41-1.88) Current vs never smokers: 0.18 (0.02-1.40)

Bibliographic reference	Klein,Ronald, Knudtson,Michael D., Cruickshanks,Karen J., Klein,Barbara E.K., Further observations on the association between smoking and the long-term incidence and progression of age-related macular degeneration: the Beaver Dam Eye Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 115-121, 2008
	Intensity, packs/d: Ever smoked: 1.19 (0.58-2.44) Duration, per 10 y Ever smoked: 1.13 (0.78-1.64) Pack-years, per 20 y Ever smoked:1.03 (0.73-1.46) Age at initiation, per 10 y Ever smoked: 0.73 (0.40-1.33) Time since quitting, per 10 y Past smokers: 0.84 (0.51-1.39) Age at quitting, per 10 y Past smokers: 1.23 (0.74-2.03) The above controlled for age, sex and baseline AMD severity level
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE

Bibliographic reference	**Klein,Ronald, Knudtson,Michael D., Cruickshanks,Karen J., Klein,Barbara E.K., Further observations on the association between smoking and the long-term incidence and progression of age-related macular degeneration: the Beaver Dam Eye Study, Archives of ophthalmology (Chicago, Ill.: 1960), 126, 115-121, 2008**
	Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis) YES

Bibliographic reference	**Klein,Ronald, Cruickshanks,Karen J., Myers,Chelsea E., Sivakumaran,Theru A., Iyengar,Sudha K., Meuer,Stacy M., Schubert,Carla R., Gangnon,Ronald E., Klein,Barbara E.K., The relationship of atherosclerosis to the 10-year cumulative incidence of age-related macular degeneration: the Beaver Dam studies, Ophthalmology, 120, 1012-1019, 2013**
Country/ies where the study was carried out	Beaver Dam, USA
Study type	Longitudinal Cohort study
Aim of the study	To describe the relationships of intima-media layer thickness, plaque in the carotid artery, angina, myocardial infarction and stroke to the 10 year cumulative incidence of early and late age-related macular degeneration and progression of AMD.

Bibliographic reference	**Klein,Ronald, Cruickshanks,Karen J., Myers,Chelsea E., Sivakumaran,Theru A., Iyengar,Sudha K., Meuer,Stacy M., Schubert,Carla R., Gangnon,Ronald E., Klein,Barbara E.K., The relationship of atherosclerosis to the 10-year cumulative incidence of age-related macular degeneration: the Beaver Dam studies, Ophthalmology, 120, 1012-1019, 2013**
Study dates	From 1998 to 2010
Source of funding	This study was supported by National Institutes of Health grants, and Research to Prevent Blindness, New York, NY. The National Eye Institute and National Institute on Aging provided funding for entire study including collection and analyses of data; RPB provided additional support for data analyses.
Number of patients	1700 persons who participated in both the Epidemiology of Hearing Loss Study and the Beaver Dam Eye Study.
Inclusion Criteria	• Persons aged 53–96 years participating in both the Epidemiology of Hearing Loss Study (EHLS) and the Beaver Dam Eye Study (BDES).
Exclusion Criteria	• Exudative AMD at baseline examination • People who did not participate in follow up • No fundus photograph that were gradable for AMD at the 1998-2000 or any follow-up exam • No carotid artery ultrasonography at the baseline examination
Diagnostic criteria	Stereoscopic 30° colour fundus photographs centred on the macula (Diabetic Retinopathy Study standard field 2) were taken of each eye. Two gradings were performed for the pair of photographs of each macula at each examination using the Wisconsin Age-Related Maculopathy Grading System. Graders were masked as to any information related to the participant and to the fellow eye. High resolution B-mode carotid artery ultrasound images were obtained using a modification of the Atherosclerosis Risk In Communities (ARIC) study ultrasound scanning protocol. The severity of AMD was determined using the modified 5-step BDES AMD Severity Scale: 10 (No AMD): Hard drusen or small soft drusen (<125 µm in diameter only) regardless of area of involvement and no pigmentary abnormalities (defined as increased retinal pigment or retinal pigment epithelial [RPE] depigmentation present); or no definite drusen with any pigmentary abnormality. 20 (Minimally severe early AMD): Hard drusen or small soft drusen (<125 µm in diameter), regardless of area of involvement, with any pigmentary abnormality; or soft drusen (≥ 125 µm in diameter) with drusen area <331,820 µm2 and no pigmentary abnormalities. 30 (Moderately severe early AMD): Soft drusen (≥ 125 µm in diameter) with drusen area <331,820 µm2 (equivalent to O2) and with any pigmentary abnormality; or soft drusen (≥ 125 µm in diameter) with drusen area ≥331,820 µm2 (equivalent to O2) with or without increased retinal pigment but no RPE depigmentation.

Bibliographic reference	**Klein,Ronald, Cruickshanks,Karen J., Myers,Chelsea E., Sivakumaran,Theru A., Iyengar,Sudha K., Meuer,Stacy M., Schubert,Carla R., Gangnon,Ronald E., Klein,Barbara E.K., The relationship of atherosclerosis to the 10-year cumulative incidence of age-related macular degeneration: the Beaver Dam studies, Ophthalmology, 120, 1012-1019, 2013**
	40 (Severe early AMD): Soft drusen (≥125 µm in diameter) with drusen area ≥331,820 µm2 (equivalent to O2) and RPE depigmentation present, with or without increased retinal pigment. 50 (Late AMD): Pure geographic atrophy (GA) in the absence of exudative macular degeneration; or exudative macular degeneration with or without GA present.
Patient characteristics	Age, years, mean (SD): 71.9 (10.7) Sex, male, 42.7%
Predictors/risk factors and effect estimates	Risk factors studied: Mean IMT, Maximum IMT, Plaque sites, History of MI present, History of stroke present, History of CVD present, History of angina present Adjusted for: Age (years), Sex (male), Mean arterial blood pressure, Hypertension present, Current smoker, Serum total cholesterol, Serum HDL, cholesterol, History of statin use, History of MI present, History of stroke present, History of CVD present, History of angina present, History of multivitamin use, Diabetes present, Body mass index, Sedentary lifestyle, Serum C-reactive protein, White blood cell count, CFH genotype, C/T, C/C, ARMS2, genotype, G/T, T/T.
Outcomes	Adjusted odds ratios for the incidence of AMD or the progression to Late AMD, Geographic atrophy or exudative AMD.
Analysis used	Discrete logistic hazard regression was used to estimate odds ratios (ORs)
Length of follow up	10 years
Missing data handling/loss to follow up	Of 2609 people 909 were excluded: Persons included in the analyses were more likely to be younger (mean age 66.8 vs. 71.8 years) than those excluded. While adjusting for age, persons excluded were more likely to lead a sedentary lifestyle, more likely to have a history of stroke or CVD, and have higher serum C-reactive protein levels and white blood cell counts. There were no statistically significant differences between persons included and persons excluded by sex, mean arterial blood pressure, body mass index, history of smoking, history of taking multivitamins, and distributions of Complement Factor H and Age-Related Maculopathy Susceptibility 2 single nucleotide polymorphisms.
Results	Adjusted odds ratios for risk of early AMD 1060 (n at risk) 161 (n of events) History of MI present 1.13 (0.60, 2.14)

Bibliographic reference	**Klein,Ronald, Cruickshanks,Karen J., Myers,Chelsea E., Sivakumaran,Theru A., Iyengar,Sudha K., Meuer,Stacy M., Schubert,Carla R., Gangnon,Ronald E., Klein,Barbara E.K., The relationship of atherosclerosis to the 10-year cumulative incidence of age-related macular degeneration: the Beaver Dam studies, Ophthalmology, 120, 1012-1019, 2013**
	History of stroke present 1.25 (0.46, 3.38) History of CVD present 0.79 (0.46, 1.37) History of angina present 0.90 (0.48, 1.71) Adjusted odds ratios for risk of late AMD 1400 (n at risk) 54 (n of events) History of MI present 1.04 (0.36, 3.02) History of CVD present 1.33 (0.59, 3.01) History of angina present 0.89 (0.32, 2.50) Adjusted odds ratios for risk of Geographic Atrophy History of MI present 0.61 (0.07, 5.34) History of CVD present 1.31 (0.32, 5.27) History of angina present 1.53 (0.30, 7.85) Adjusted odds ratios Exudative AMD History of MI present 1.56 (0.48, 5.08) History of CVD present 1.66 (0.65, 4.26) History of angina present 0.92 (0.27, 3.13) Adjusted for all factors as well as BMI, smoking status, history of multivitamin use, serum high-density lipoprotein cholesterol and C-reactive protein levels, hypertension status, diabetes status, history of statin use, white blood cell count, and CFH and ARMS2 genotypes.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors

Bibliographic reference	**Klein,Ronald, Cruickshanks,Karen J., Myers,Chelsea E., Sivakumaran,Theru A., Iyengar,Sudha K., Meuer,Stacy M., Schubert,Carla R., Gangnon,Ronald E., Klein,Barbara E.K., The relationship of atherosclerosis to the 10-year cumulative incidence of age-related macular degeneration: the Beaver Dam studies, Ophthalmology, 120, 1012-1019, 2013**
	Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). YES Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis) YES

Bibliographic reference	**Knudtson,M.D., Klein,R., Klein,B.E., 20061211, Physical activity and the 15-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, British Journal of Ophthalmology, 90, 1461-1463, 2006**
Country/ies where the study was carried out	Beaver Dam, USA

Bibliographic reference	Knudtson,M.D., Klein,R., Klein,B.E., 20061211, Physical activity and the 15-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, British Journal of Ophthalmology, 90, 1461-1463, 2006
Study type	Longitudinal Cohort Study
Aim of the study	To explore the relationship between physical activity and the long term incidence of AMD
Study dates	1988-2003
Source of funding	This study was supported by the National Institutes of Health grant and partly by the Research to Prevent Blindness
Number of patients	4,926 persons 3,684 participated in 5 year follow up 2,764 participated in 10 year follow up 2,119 participated in 15 year follow up examinations
Inclusion Criteria	A private census of the population of Beaver Dam, Wisconsin All residents aged 43- 84 years
Exclusion Criteria	None stated
Diagnostic criteria	Fundus photographs of the retina were obtained at each examination and graded in a blinded fashion using the Wisconsin Age-Related Maculopathy Grading System to determine the AMD status. Early AMD was defined as presence of soft indistinct drusen or pigmentary abnormalities in the presence of drusen. Geographic atrophy (pure form) and exudative AMD were defined according to the standard definitions. Participants were asked three questions on physical activity: ‘‘On average, how many flights of stairs do you climb each day?’’; ‘‘On average, how many city blocks do you walk each day?’’; ‘‘At least once a week, do you engage in a regular activity long enough to work up a sweat?’’ and if so, ‘‘How many times per week do you do this?’’ For the purpose of analyses, stair climbing was categorised as none, 1–3 flights, 4–6 flights, .6 flights/day; walking was categorised as none, 1–4 blocks, 5–12 blocks, .12 blocks/day; active lifestyle was defined as engaging in regular activity with or without sweating >3 times/week; and sedentary lifestyle was defined as regular activity 3 times/week.
Patient characteristics	Age at baseline (n=4755) 43- 54: 1500 55-64: 1295 65-74: 1242

Bibliographic reference	Knudtson,M.D., Klein,R., Klein,B.E., 20061211, Physical activity and the 15-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, British Journal of Ophthalmology, 90, 1461-1463, 2006
	75-86: 718 Gender (n): Women: 2642 Men: 2113 Ethnicity: 99% white
Predictors/risk factors and effect estimates	Risk factors under study were Active/sedentary lifestyle, stair climbing, walking Multivariate odds ratios (ORs) adjusted for age, sex, history of arthritis, systolic blood pressure, smoking, education and body mass index
Outcomes	Adjusted odds ratios for developing early AMD Adjusted odds ratios for developing geographic atrophy Adjusted odds ratios for developing exudative AMD
Analysis used	Discrete logistic hazard regression.
Length of follow up	15 years
Missing data handling/loss to follow up	In general, persons who did not participate in the 15-year follow-up were older at baseline than those who did. After adjusting for age, persons who did not participate were more likely to have fewer years of education completed and higher systolic blood pressure than persons who participated. All those who contributed some follow-up information at the baseline examination were included in the analysis (n=3874).
Results	Odds of early AMD (adjusted odds ratios) Exercise status Sedentary: reference Active: 0.9 (0.7 to 1.1) Odds of Geographic atrophy (adjusted odds ratios) Exercise status

Bibliographic reference	Knudtson,M.D., Klein,R., Klein,B.E., 20061211, Physical activity and the 15-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, British Journal of Ophthalmology, 90, 1461-1463, 2006
	Sedentary: reference Active: 1.1 (0.5 to 2.3) Odds of exudative AMD Exercise status Sedentary: reference Active: 0.3 (0.1 to 0.7) Above adjusted for age, sex, arthritis, systolic blood pressure, body mass index, smoking and education.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). NO (disputable cut points, definitions) Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY

Bibliographic reference	Knudtson,M.D., Klein,R., Klein,B.E., 20061211, Physical activity and the 15-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study, British Journal of Ophthalmology, 90, 1461-1463, 2006
	The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis) YES

Bibliographic reference	Lechanteur,Yara T.E., van de Ven,Johannes P.H., Smailhodzic,Dzenita, Boon,Camiel J.F., Klevering,B.Jeroen, Fauser,Sascha, Groenewoud,Joannes M.M., van der Wilt,Gert-Jan, den Hollander,Anneke I., Hoyng,Carel B., Genetic, behavioral, and sociodemographic risk factors for second eye progression in age-related macular degeneration, Investigative ophthalmology & visual science, 53, 5846-5852, 2012
Country/ies where the study was carried out	Netherlands
Study type	Retrospective cohort study
Aim of the study	To investigate the correlation of genetic, sociodemographic, and behavioural risk factors with second eye progression to end-stage AMD.
Study dates	All 108 subjects were selected by means of chart review from the European Genetic Database (EUGENDA) and were entered into the database between January 1997 and December 2006. EUGENDA is a multicentre database of AMD patients and control subjects founded by the Radboud University Nijmegen Medical Centre and the University of Cologne Medical Centre.
Source of funding	Supported by MD fonds, Oogfonds, and Algemene Nederlandse Vereniging ter Voorkoming van Blindheid.
Number of patients	191 patients were selected according to inclusion criteria 83 patients were excluded 108 patients remained
Inclusion Criteria	• End-stage AMD in one or both eyes
Exclusion Criteria	• No end-stage AMD in both eyes; • Unknown or unclear time of end-stage AMD in one or both eyes; • Other retinal diseases that interfered with the diagnosis of end-stage AMD, such as central serous chorioretinopathy;

Bibliographic reference	**Lechanteur,Yara T.E., van de Ven,Johannes P.H., Smailhodzic,Dzenita, Boon,Camiel J.F., Klevering,B.Jeroen, Fauser,Sascha, Groenewoud,Joannes M.M., van der Wilt,Gert-Jan, den Hollander,Anneke I., Hoyng,Carel B., Genetic, behavioral, and sociodemographic risk factors for second eye progression in age-related macular degeneration, Investigative ophthalmology & visual science, 53, 5846-5852, 2012**
	• Laser treatment or radiotherapy for a retinal disease or treatment for AMD in a stage that could not be determined as end-stage (e.g., laser therapy for extensive drusen).
Diagnostic criteria	Colour fundus photographs and fluorescein angiography images were taken with a digital fundus camera. End-stage AMD was defined as either choroidal neovascularization within the central 6 mm ETDRS grid or geographic atrophy of an area of at least 175 µm including the fovea. Development of advanced AMD in the first eye was taken as starting-point (T[0]) and had to be known with an accuracy range of 1 month; an accuracy range of 6 months was accepted if the second eye did not develop end-stage AMD within 4 years. Progression time until the development of end-stage AMD in the fellow eye was calculated in months after T(0).
Patient characteristics	Mean age was 74.3 years (range 54.3–93.4; standard deviation ±7.2) in our studied cohort. There were 37 males (34.3%) and 71 females (65.7%). The type of end-stage AMD in the first eye was CNV in 82.4% and GA in 3.7% of cases.
Predictors/risk factors and effect estimates	Sex, Age, BMI, cigarette smoking (pack years), education level and various genetic SNPs were the risk factors of interest. hazard ratios were corrected for sex, age, BMI and pack years (statistically significant at univariate level)
Outcomes	Association between socioeconomic risk factors and progression towards end-stage AMD in the Fellow eye of patients with unilateral advanced AMD.
Analysis used	Variables were entered in a Cox regression model for survival analysis and were first analysed in a univariate model. Statistically significant variables ($P < 0.05$) were analysed in a multivariate model.
Length of follow up	4 years
Missing data handling/loss to follow up	Of 191 eligible participants, 83 were subsequently excluded for the following reasons: Passed away (n=22) Could not be contacted (n=42) Discrepancy between patients story and chart information (n=5) Unwilling to participate (n=4) No information received (n=10)

Bibliographic reference	**Lechanteur,Yara T.E., van de Ven,Johannes P.H., Smailhodzic,Dzenita, Boon,Camiel J.F., Klevering,B.Jeroen, Fauser,Sascha, Groenewoud,Joannes M.M., van der Wilt,Gert-Jan, den Hollander,Anneke I., Hoyng,Carel B., Genetic, behavioral, and sociodemographic risk factors for second eye progression in age-related macular degeneration, Investigative ophthalmology & visual science, 53, 5846-5852, 2012**
Results	Hazard ratios for progression towards end-stage AMD in the Fellow eye of patients with unilateral advanced AMD. (95% confidence intervals) Sex Male: 1.0 (reference) Female: 2.6 (1.4–5.0) Age, years <65: 1.0 (reference) 65 to 70: 1.2 (0.5–2.7) 70 to 75: 1.5 (0.7–3.1) 75 to 80: 2.6 (1.3–5.3) ≥80: 5.0 (2.0–12.5) BMI Normal weight (18–25): 1.0 (reference) Overweight (25–30):1.3 (0.8–2.1) Obese (≥30): 2.2 (1.1–4.1) Pack years 0 to 1: 1.0 (reference) 1 to 40: 2.4 (1.3–4.5) ≥40: 4.4 (1.4–14.3) Education ≤ High school: 1.0 (reference) > High school: 0.6 (0.4–1.1)

Bibliographic reference	**Lechanteur,Yara T.E., van de Ven,Johannes P.H., Smailhodzic,Dzenita, Boon,Camiel J.F., Klevering,B.Jeroen, Fauser,Sascha, Groenewoud,Joannes M.M., van der Wilt,Gert-Jan, den Hollander,Anneke I., Hoyng,Carel B., Genetic, behavioral, and sociodemographic risk factors for second eye progression in age-related macular degeneration, Investigative ophthalmology & visual science, 53, 5846-5852, 2012**
	Hazard ratios corrected for sex, age, BMI, and Pack years.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis) YES

Bibliographic reference	Reynolds,Robyn, Rosner,Bernard, Seddon,Johanna M., Dietary omega-3 fatty acids, other fat intake, genetic susceptibility, and progression to incident geographic atrophy, Ophthalmology, 120, 1020-1028, 2013
Country/ies where the study was carried out	USA
Study type	Prospective longitudinal cohort study
Aim of the study	To investigate associations between dietary omega-3 fatty acids and other fat intake, genes related to age-related macular degeneration (AMD) and progression to geographic atrophy (GA)
Study dates	Published 2012 AREDs trial: 1992 start with follow up until 2005
Source of funding	Supported by in part by Grants from the National Institutes of Health; Massachusetts Lions Eye Research Fund, Inc.; Unrestricted grant from Research to Prevent Blindness, Inc; the American Macular Degeneration Foundation; and the Macular Degeneration Research Fund of the Ophthalmic Epidemiology and Genetics Service.
Number of patients	2128 individuals (4165 eyes)
Inclusion Criteria	• Age 55-80 years • At least one eye had to be free from vision-threatening disease other than AMD and cataract • That eye could not have had surgery, except for cataract surgery • The participants' stages of disease ranged from no evidence of AMD in either eye, to advanced AMD with vision loss in one eye but good vision (at least 20/30) in the other eye. • Eyes had media that were sufficiently clear to obtain adequate-quality stereoscopic fundus photographs of the macula.
Exclusion Criteria	• Eyes with the end point (4 or 5) at baseline were excluded from the analysis. • Individuals with intake < 600 were excluded from the analysis and, men and women with total caloric intake ≥4200 or ≥3200, respectively, were excluded from the analyses.
Diagnostic criteria	Eyes were assigned a grade of no AMD, early, intermediate, or two different forms of advanced or late stage AMD based on the 5 Stage Clinical Age-Related Maculopathy Grading System (CARMS), in order to combine central and non-central GA into one grade, and to separate NV as a separate grade, regardless of visual acuity. Grades were defined as follows based on fundus and examination data: Neovascular disease, or grade 5, if there were any definitive signs of neovascular AMD such as haemorrhagic retinal detachment, haemorrhage under the retina or retinal pigment epithelium, or subretinal fibrosis;

Bibliographic reference	Reynolds,Robyn, Rosner,Bernard, Seddon,Johanna M., Dietary omega-3 fatty acids, other fat intake, genetic susceptibility, and progression to incident geographic atrophy, Ophthalmology, 120, 1020-1028, 2013
	Geographic atrophy, or grade 4 if there was geographic atrophy either in the centre grid or anywhere within the grid and had no record of haemorrhage; Large drusen (≥125µm) were assigned to grade 3; Intermediate drusen (63–124µm) were assigned to grade 2, as long as there were no signs of advanced AMD; No drusen or only a few small drusen (<63µm) were assigned to grade 1. Progression was defined as either eye progressing from a grade 1, 2, or 3 to grade 4 (GA), at any point in time. Eyes with the end point (4 or 5) at baseline were excluded from the analysis. Follow-up ended when an eye progressed to GA. Eyes that had no record of GA were censored when they reached grade 5
Patient characteristics	AREDs cohort (n= 2914) Age, y, n <65: 565 65-74: 1899 ≥75: 450 Sex Female: 1648 Male: 1266 Ethnicity- not described Baseline characteristics of the sample used for this study were not described.
Predictors/risk factors and effect estimates	Risk factors under study: Demographic (age and sex), behavioural (BMI, smoking, antioxidant status), and dietary information at baseline was obtained from dbGAP. Antioxidant treatment was defined as “yes” for subjects in the antioxidants alone or the antioxidants plus zinc groups, and “no” for subjects in the placebo or the zinc groups. Antioxidant treatment groups were randomly assigned in the AREDS clinical trial. Diet data were obtained from food frequency questionnaires (FFQs),

Bibliographic reference	Reynolds,Robyn, Rosner,Bernard, Seddon,Johanna M., Dietary omega-3 fatty acids, other fat intake, genetic susceptibility, and progression to incident geographic atrophy, Ophthalmology, 120, 1020-1028, 2013
	including measurements of total fat, saturated fat, total polyunsaturated fatty acids, monounsaturated fat, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), combined long chain polyunsaturated fatty acids DHA and EPA, linolenic, and linoleic acid (an omega-6 fatty acid). Models were adjusted for the following factors: baseline AMD status, genetic, environmental, demographic, and dietary fat intake.
Outcomes	Hazard ratios (HR) and 95% confidence intervals (CI) for progression to geographic atrophy in individual eyes
Analysis used	Cox proportional hazards model
Length of follow up	Up to 12 years of follow up
Missing data handling/loss to follow up	Unclear (none described)
Results	Multivariate Associations Between Dietary Fats and Progression to Geographic Atrophy, hazard ratios, (95% confidence intervals) Total Fat (g) Quintile 1: 1.0 Quintile 2: 1.14 (0.82 – 1.59) Quintile 3: 0.99 (0.70 – 1.39) Quintile 4: 1.54 (1.13 – 2.11) Quintile 5: 1.18 (0.85 – 1.64) Saturated Fat (g) Quintile 1: 1.0 Quintile 2: 1.09(0.78 – 1.51) Quintile 3: 1.42 (1.03 – 1.95) Quintile 4: 1.18 (0.85 – 1.64) Quintile 5: 1.19 (0.87 – 1.64) Monounsaturated Fat (g)

Bibliographic reference	Reynolds,Robyn, Rosner,Bernard, Seddon,Johanna M., Dietary omega-3 fatty acids, other fat intake, genetic susceptibility, and progression to incident geographic atrophy, Ophthalmology, 120, 1020-1028, 2013
	Quintile 1: 1.0 Quintile 2: 1.37 (0.98 – 1.91) Quintile 3: 1.22 (0.86 – 1.71) Quintile 4: 1.38 (0.99 – 1.94) Quintile 5: 1.47 (1.05 – 2.05) Total Polyunsaturated Fatty Acids (g) Quintile 1: 1.0 Quintile 2: 0.95 (0.68 – 1.33) Quintile 3: 1.10 (0.80 – 1.52) Quintile 4: 1.34 (0.97 –1.85) Quintile 5: 1.13 (0.82 – 1.55) Omega-3 Fatty Acids Eicosapentaenoic Acid (EPA)(g) Quintile 1: 1.0 Quintile 2: 0.92 (0.65 – 1.30) Quintile 3: 1.16 (0.86 – 1.58) Quintile 4: 1.00 (0.71 – 1.39) Quintile 5: 0.84 (0.59 – 1.18) Docosahexaenoic Acid (DHA)(g) Quintile 1: 1.0 Quintile 2: 0.99 (0.73 – 1.36) Quintile 3: 1.14 (0.84 – 1.53) Quintile 4: 0.93 (0.68 – 1.27) Quintile 5: 0.72 (0.52 – 1.01) DHA + EPA (g) Quintile 1: 1.0

Bibliographic reference	Reynolds,Robyn, Rosner,Bernard, Seddon,Johanna M., Dietary omega-3 fatty acids, other fat intake, genetic susceptibility, and progression to incident geographic atrophy, Ophthalmology, 120, 1020-1028, 2013
	Quintile 2: 0.98 (0.70 – 1.38) Quintile 3: 1.20 (0.88 – 1.64) Quintile 4: 0.91 (0.64 – 1.29) Quintile 5: 0.79 (0.55 – 1.12) Linolenic Acid (g) Quintile 1: 1.0 Quintile 2: 0.90 (0.64 – 1.23) Quintile 3: 1.02 (0.74 – 1.42) Quintile 4: 1.06 (0.77 – 1.47) Quintile 5: 1.08(0.80 – 1.46) Omega-6 Fatty Acids Linoleic Acid (g) Quintile 1: 1.0 Quintile 2: 0.98 (0.70 – 1.37) Quintile 3: 1.04 (0.75 – 1.44) Quintile 4: 1.36 (0.99 – 1.87) Quintile 5: 1.11 (0.81 – 1.53) Arachidonic Acid (g) Quintile 1: 1.0 Quintile 2: 0.92 (0.67 – 1.26) Quintile 3: 0.85 (0.62 – 1.17) Quintile 4: 0.91 (0.66 – 1.25) Quintile 5: 0.84 (0.62 – 1.14) Hazard ratios adjusted for: baseline grade, demographic and environmental characteristics: age, gender, education, smoking, antioxidants and body mass index
Limitations	Quality assessment criteria for prognostic studies as outlined in:

Bibliographic reference	Reynolds,Robyn, Rosner,Bernard, Seddon,Johanna M., Dietary omega-3 fatty acids, other fat intake, genetic susceptibility, and progression to incident geographic atrophy, Ophthalmology, 120, 1020-1028, 2013
	Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). UNSURE Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Sandberg,M.A., Weiner,A., Miller,S., Gaudio,A.R., 19980319, High-risk characteristics of fellow eyes of patients with unilateral neovascular age-related macular degeneration, Ophthalmology, 105, 441-447, 1998
Country/ies where the study was carried out	USA
Study type	Prospective cohort study

Bibliographic reference	Sandberg,M.A., Weiner,A., Miller,S., Gaudio,A.R., 19980319, High-risk characteristics of fellow eyes of patients with unilateral neovascular age-related macular degeneration, Ophthalmology, 105, 441-447, 1998
Aim of the study	To determine whether clinical tests of ocular function and macular appearance independently can help to predict which patients with unilateral neovascular age-related AMD will have a choroidal neovascular membrane develop in their fellow eye.
Study dates	Published 1997 Data collected 1990 to 1995
Source of funding	Grants from National Eye Institute, the Foundation for Fighting Blindness and the Massachusetts Lions Eye Research Fund, Inc.
Number of patients	127 patients with unilateral neovascular AMD
Inclusion Criteria	• Snellen visual acuity of 20/60 or better in the fellow eye with sufficiently clear media to allow adequate visualisation of the fundus. • The presence of a choroidal neovascular membrane in the macular of the affected eye • Macular drusen in both eyes • No sign of other retinal disease
Exclusion Criteria	• Bilateral dry AMD • Bilateral Neovascular AMD • Choroidal neovascularisation associated with high myopia
Diagnostic criteria	On the study eye, best corrected visual acuity was measured using a Snellen chart. Mucular visual field was assessed by letter recognition perimetry Foveal glare recovery time was assessed by photostress testing Foveal electroretinograms were recorded with a hand-held stimulator ophthalmoscope. Measurements of ocular function, biomicroscopy and direct and indirect ophthalmoscopy were performed and photographs of each macular were obtained. Fluorescein angiography was performed if a recent one was unavailable. Or if the fundus showed recent changes that could be attributable to choroidal neovascularisation.
Patient characteristics	Age: median 74 years Gender: 57 men, 70 women

Bibliographic reference	Sandberg,M.A., Weiner,A., Miller,S., Gaudio,A.R., 19980319, High-risk characteristics of fellow eyes of patients with unilateral neovascular age-related macular degeneration, Ophthalmology, 105, 441-447, 1998
	Ethnicity: not described
Predictors/risk factors and effect estimates	Risk factors assessed were: age, spherical equivalent, glare recovery time, focal electroretinal implicit time, No. of large drusen (quartiles 1-4), macular appearance grade. Prognostic factors entered into the analysis were: age, body mass index, blood pressure, spherical equivalent, Snellen acuity, STDRS acuity, number of visual field defects, glare recovery time, foveal electroretinogram amplitude, foveal electroretinogram implicit time, and grade of macular appearance.
Outcomes	Relative risk of developing a choroidal neovascular membrane.
Length of follow up	4.5 years follow up Follow up visits every 6 months
Missing data handling/loss to follow up	93 people from the initial 127 had been lost to follow up and were censored by the end of 4.5 years.
Results	Relative risk of choroidal neovascular membrane Age, y, continuous (95% confidence intervals) RR: 1.08 (1.02-1.14) No. of large drusen, quartile (95% confidence interval) Quartile 1: reference Quartile 2: 2.09 (0.66-7.84) Quartile 3: 0.83 (0.20-3.52) Quartile 4: 3.25 (1.11-11.75)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE

Bibliographic reference	Sandberg,M.A., Weiner,A., Miller,S., Gaudio,A.R., 19980319, High-risk characteristics of fellow eyes of patients with unilateral neovascular age-related macular degeneration, Ophthalmology, 105, 441-447, 1998
	Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). NO Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Seddon,Johanna M., Cote,Jennifer, Rosner,Bernard, Progression of age-related macular degeneration: association with dietary fat, transunsaturated fat, nuts, and fish intake, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 1728-1737, 2003
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To advise patients with a high risk for advanced forms of AMD about preventive measures through our evaluation of the relationship between dietary alterations and the progression of early or intermediate AMD to the advanced stages of the disease associated with visual loss.
Study dates	Between July 1989 and May 1998,

Bibliographic reference	**Seddon,Johanna M., Cote,Jennifer, Rosner,Bernard, Progression of age-related macular degeneration: association with dietary fat, transunsaturated fat, nuts, and fish intake, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 1728-1737, 2003**
Source of funding	This study was supported by grants from the Foundation Fighting Blindness Inc, Owings Mills, Md; the Massachusetts Lions Eye Research Fund Inc, Northboro; Research to Prevent Blindness Inc, New York, NY; the Epidemiology Unit Research Fund, Massachusetts Eye and Ear Infirmary, Boston; and a Lew R. Wasserman Merit Award from Research to Prevent Blindness.
Number of patients	397 people were eligible for enrolment 366 (92%) enrolled n=261
Inclusion Criteria	• Patients with AMD, seen for examination at the Massachusetts Eye and Ear Infirmary, Boston. • Other inclusion criteria included willingness to participate in a long-term study that involved annual dilated eye examinations and fundus photography.
Exclusion Criteria	• Unable to speak English • Decreased hearing or cognitive function such that they would not be able to understand a health status and dietary interview.
Diagnostic criteria	Stereoscopic colour fundus photographs of the macula were obtained. They used a 5-grade classification scale of AMD, modified from the Age-Related Eye Disease Study grading system. Macular characteristics were graded within a 3000-µm radius centred on the foveal centre. Eyes with extensive small drusen (15 small drusen; 63 µm), non-extensive intermediate drusen (20 drusen; 63 µm but 125 µm), or pigment abnormalities associated with AMD were assigned a grade of. Eyes with extensive intermediate or large (125-µm) drusen were assigned a grade of 3. Eyes with geographic atrophy received a grade of 4. If there was evidence of retinal pigment epithelial detachment or choroidal neovascular membrane, a grade of 5 was assigned. Eyes received a grade of 1 if none of these signs was present. Advanced AMD is defined as grades 4 and 5. To evaluate intergrader reliability, fundus photographs of participants with at least 3 years of follow-up (n=222) were sent to the Wisconsin Fundus Photographic Reading Center, Madison, for detailed age-related maculopathic grading.
Patient characteristics	Subjects were aged 60 years and older, were primarily white (99.9%), and had at least 1 eye with a best corrected visual acuity of 20/200 or better and non-exudative AMD.

Bibliographic reference	**Seddon,Johanna M., Cote,Jennifer, Rosner,Bernard, Progression of age-related macular degeneration: association with dietary fat, transunsaturated fat, nuts, and fish intake, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 1728-1737, 2003**
Predictors/risk factors and effect estimates	Risk factors under study include: intake of nuts, fish, meat, saturated and unsaturated fat and processed baked goods. Multivariable analysis was adjusted for: age-sex group adjusted for age-sex group (men aged 60-69 years, men aged 70-79 years, men aged ≥80 years, women aged 60-69 years, women aged 70-79 years, women aged ≥80 years), log energy (continuous), log carotenoid intake (continuous), initial AMD grade (categorical), and education (at least less than high school).
Outcomes	Relative Risks for Progression to Advanced Age-Related Macular Degeneration by Quartiles of Fat Intake Relative Risks for Progression to Advanced Age-Related Macular Degeneration by Energy-Adjusted Quartiles of Various Types of Saturated and Unsaturated Fat Relative Risks for Progression to Advanced Age-Related Macular Degeneration by Frequency of Fish Intake Relative Risks for Progression to Advanced Age-Related Macular Degeneration According to Intake of Select Food Groups: high fat dairy; meat, processed baked goods. Relative Risks for Progression to Advanced Age-Related Macular Degeneration According to Intake of Nuts
Analysis used	The principal method of analysis was the Cox proportional hazards model.
Length of follow up	Average follow up time was 4.6 years
Missing data handling/loss to follow up	Of the 366 participants enrolled 36 were not considered for analyses because of: Inability to complete the initial study examination (n=5), Lack of follow-up data (n=17), Lack of 1 or more primary independent variables (n=14) Nineteen individuals (7%) were lost to follow-up because of unwillingness to return for additional follow-up examinations. These individuals did not differ significantly from the remaining participants (n=242) with regard to age or education; however, significantly more women were lost to follow-up (10%) compared with men (3%).
Results	Relative Risks for Progression to Advanced Age-Related Macular Degeneration by Quartiles of Fat Intake: (95% confidence intervals)

Bibliographic reference	Seddon,Johanna M., Cote,Jennifer, Rosner,Bernard, Progression of age-related macular degeneration: association with dietary fat, transunsaturated fat, nuts, and fish intake, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 1728-1737, 2003
	Total fat 1st quartile: 1.0 2nd quartile: 1.27 (0.63-2.53) 3rd quartile: 2.29 (1.08-4.88) 4th quartile: 2.90 (1.15-7.32) Animal fat 1st quartile: 1.0 2nd quartile: 0.81 (0.41-1.57) 3rd quartile: 1.14 (0.55-2.37) 4th quartile: 2.29 (0.91-5.72) Vegetable fat 1st quartile: 1.0 2nd quartile: 1.64 (0.86-3.13) 3rd quartile: 2.27 (1.12-4.59) 4th quartile: 3.82 (1.58-9.28) Saturated fat 1st quartile: 1.0 2nd quartile: 0.97 (0.49-1.93) 3rd quartile: 1.46 (0.66-3.20) 4th quartile: 2.09 (0.83-5.28) Monounsaturated fat 1st quartile: 1.0

Bibliographic reference	Seddon,Johanna M., Cote,Jennifer, Rosner,Bernard, Progression of age-related macular degeneration: association with dietary fat, transunsaturated fat, nuts, and fish intake, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 1728-1737, 2003
	2nd quartile: 1.27 (0.65-2.45) 3rd quartile: 2.13 (1.03-4.43) 4th quartile: 2.21 (0.90-5.47) Polyunsaturated fat 1st quartile: 1.0 2nd quartile: 1.57 (0.82-3.02) 3rd quartile: 1.90 (0.94-3.84) 4th quartile: 2.28 (1.04-4.99) Transunsaturated fat 1st quartile: 1.0 2nd quartile: 1.67 (0.83-3.36) 2nd quartile: 3.22 (1.63-6.36) 3rd quartile: 2.39 (1.10-5.17) Relative Risks for Progression to Advanced Age-Related Macular Degeneration by Frequency of Fish Intake (95% confidence intervals) Number of servings of fish a week <1: 1.0 1: 1.30 (0.78-2.16) ≥2: 0.88 (0.49-1.60) Relative Risks for Progression to Advanced Age-Related Macular Degeneration by type of food group (95% confidence intervals)

Bibliographic reference	Seddon,Johanna M., Cote,Jennifer, Rosner,Bernard, Progression of age-related macular degeneration: association with dietary fat, transunsaturated fat, nuts, and fish intake, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 1728-1737, 2003
	High-fat dairy 1st quartile: 1.0 2nd quartile: 2.08 (1.09-3.97) 3rd quartile: 1.80 (0.96-3.38) 4th quartile: 1.91 (0.98-3.73) Meat 1st quartile: 1.0 2nd quartile: 1.75 (0.91-3.34) 3rd quartile: 1.62 (0.81-3.24) 4th quartile: 2.09 (0.98-4.47) Processed baked goods 1st quartile: 1.0 2nd quartile: 1.21 (0.69-2.26) 3rd quartile: 2.02 (1.06-3.85) 4th quartile: 2.42 (1.21-4.84) Relative Risks for Progression to Advanced Age-Related Macular Degeneration by number of servings of nuts per week (95% confidence intervals) <1: 1.0 1: 0.69 (0.40-1.17) ≥2: 0.60 (0.32-1.02) Above risk ratios adjusted for Adjusted for age-sex group (men aged 60-69 years, men aged 70-79 years, men aged 80 years, women aged 60-69 years, women aged 70-79 years, women aged 80 years), education (high school vs high school),

Bibliographic reference	**Seddon,Johanna M., Cote,Jennifer, Rosner,Bernard, Progression of age-related macular degeneration: association with dietary fat, transunsaturated fat, nuts, and fish intake, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 1728-1737, 2003**
	smoking (current, past, or never), body mass index (25, 25-29.9, or 30), systolic blood pressure, cardiovascular disease, log energy (continuous), protein intake (quartile), energy-adjusted log beta carotene intake (continuous), alcohol intake (continuous), physical activity (continuous, mean number of times per week of vigorous activity), and initial age-related macular degeneration grade (categorical), total intake of energy-adjusted log zinc, vitamin C, and vitamin E.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNCLEAR Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). PARTLY Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Seddon,Johanna M., Cote,Jennifer, Davis,Nancy, Rosner,Bernard, Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 785-792, 2003**
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To advise patients with a high risk for advanced forms of AMD about preventive measures through our evaluation of the relationship between different variables and the progression of early or intermediate AMD to the advanced stages of the disease associated with visual loss.
Study dates	Between July 1989 and May 1998
Source of funding	This study was supported by grants from the Foundation Fighting Blindness Inc, Owings Mills, Md; the Massachusetts Lions Eye Research Fund Inc, Northboro; Research to Prevent Blindness Inc, New York, NY; the Epidemiology Unit Research Fund, Massachusetts Eye and Ear Infirmary, Boston; and a Lew R. Wasserman Merit Award from Research to Prevent Blindness.
Number of patients	397 people were eligible for enrolment 366 (92%) enrolled n=261
Inclusion Criteria	• Patients with AMD, seen for examination at the Massachusetts Eye and Ear Infirmary, Boston. • Other inclusion criteria included willingness to participate in a long-term study that involved annual dilated eye examinations and fundus photography.
Exclusion Criteria	• Unable to speak English • Decreased hearing or cognitive function such that they would not be able to understand a health status and dietary interview.
Diagnostic criteria	Stereoscopic colour fundus photographs of the macula were obtained. They used a 5-grade classification scale of AMD, which we modified from the Age-Related Eye Disease Study grading system. Macular characteristics were graded within a 3000-µm radius centred on the foveal centre. Eyes with extensive small drusen (15 small drusen; 63 µm), non-extensive intermediate drusen (20 drusen; 63 µm but 125 µm), or pigment abnormalities associated with AMD were assigned a grade of. Eyes with extensive intermediate or large (125-µm) drusen were assigned a grade of 3. Eyes with geographic atrophy received a grade of 4. If there was evidence of retinal pigment epithelial detachment or choroidal neovascular

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	membrane, a grade of 5 was assigned. Eyes received a grade of 1 if none of these signs was present. Advanced AMD is defined as grades 4 and 5. To evaluate intergrader reliability, fundus photographs of participants with at least 3 years of follow-up (n=222) were sent to a reading centre for detailed age-related maculopathic grading.
Patient characteristics	Subjects were aged 60 years and older, were primarily white (99.9%), and had at least 1 eye with a best corrected visual acuity of 20/200 or better and non-exudative AMD.
Predictors/risk factors and effect estimates	Risk factors under study include: BMI, Physical activity, smoking, Cardiovascular disease Multivariable analysis was adjusted for: age-sex group (men aged 60-69 years, men aged 70-79 years, men aged 80 years, women aged 60-69 years, women aged 70-79 years, women aged 80 years), education (high school vs high school), smoking (current, past, or never), body mass index (25, 25-29.9, or 30), systolic blood pressure, cardiovascular disease, log energy (continuous), protein intake (quartile), energy-adjusted log beta carotene intake (continuous), alcohol intake (continuous), physical activity (continuous, mean number of times per week of vigorous activity), and initial age-related macular degeneration grade (categorical), total intake of energy-adjusted log zinc, vitamin C, and vitamin E.
Outcomes	Relative Risks for Progression of AMD using measures of BMI, Physical activity, smoking, Cardiovascular disease
Analysis used	Cox proportional hazards model
Length of follow up	Average follow up time was 4.6 years
Missing data handling/loss to follow up	Of the 366 participants enrolled 36 were not considered for analyses because of: Inability to complete the initial study examination (n=5), Lack of follow-up data (n=17), Lack of 1 or more primary independent variables (n=14) Nineteen individuals (7%) were lost to follow-up because of unwillingness to return for additional follow-up examinations. These individuals did not differ significantly from the remaining participants (n=242) with regard to age or education; however, significantly more women were lost to follow-up (10%) compared with men (3%).

Bibliographic reference	**Seddon,Johanna M., Cote,Jennifer, Davis,Nancy, Rosner,Bernard, Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 785-792, 2003**
Results	Relative risk for progression of AMD from multivariate models including measures of obesity and other risk factors (95% Confidence Intervals) BMI <25: 1.0 (reference) 25-29: 2.32 (1.32-4.07) ≥30: 2.35 (1.27-4.34) Physical activity (vigorous activity 3 times a week): 0.75 (0.57-1.01) Smoking Never: 1.0 (reference) Past: 1.32 (0.82- 2.12) Current: 1.99 (0.90- 4.43) Cardiovascular disease: No: 1.0 (reference) Yes: 1.21 (0.73-2.02) Adjusted for age-sex group (men aged 60-69 years, men aged 70-79 years, men aged 80 years, women aged 60-69 years, women aged 70-79 years, women aged 80 years), education (high school vs high school), smoking (current, past, or never), body mass index (25, 25-29.9, or 30), systolic blood pressure, cardiovascular disease, log energy (continuous), protein intake (quartile), energy-adjusted log beta carotene intake (continuous), alcohol intake (continuous), physical activity (continuous, mean number of times per week of vigorous activity), and initial age-related macular degeneration grade (categorical), total intake of energy-adjusted log zinc, vitamin C, and vitamin E.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors

Bibliographic reference	Seddon,Johanna M., Cote,Jennifer, Davis,Nancy, Rosner,Bernard, Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 785-792, 2003
	Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNCLEAR Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). PARTLY Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Seddon,Johanna M., Cote,Jennifer, Davis,Nancy, Rosner,Bernard, Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 785-792, 2003
Country/ies where the study was carried out	USA
Study type	Prospective cohort study

Bibliographic reference	**Seddon,Johanna M., Cote,Jennifer, Davis,Nancy, Rosner,Bernard, Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 785-792, 2003**
Aim of the study	To advise patients with a high risk for advanced forms of AMD about preventive measures through our evaluation of the relationship between different variables and the progression of early or intermediate AMD to the advanced stages of the disease associated with visual loss.
Study dates	Between July 1989 and May 1998
Source of funding	This study was supported by grants from the Foundation Fighting Blindness Inc, Owings Mills, Md; the Massachusetts Lions Eye Research Fund Inc, Northboro; Research to Prevent Blindness Inc, New York, NY; the Epidemiology Unit Research Fund, Massachusetts Eye and Ear Infirmary, Boston; and a Lew R. Wasserman Merit Award from Research to Prevent Blindness.
Number of patients	397 people were eligible for enrolment 366 (92%) enrolled n=261
Inclusion Criteria	• Patients with AMD, seen for examination at the Massachusetts Eye and Ear Infirmary, Boston. • Other inclusion criteria included willingness to participate in a long-term study that involved annual dilated eye examinations and fundus photography.
Exclusion Criteria	• Unable to speak English • Decreased hearing or cognitive function such that they would not be able to understand a health status and dietary interview.
Diagnostic criteria	Stereoscopic colour fundus photographs of the macula were obtained. They used a 5-grade classification scale of AMD, which we modified from the Age-Related Eye Disease Study grading system. Macular characteristics were graded within a 3000-µm radius centred on the foveal centre. Eyes with extensive small drusen (15 small drusen; 63 µm), non-extensive intermediate drusen (20 drusen; 63 µm but 125 µm), or pigment abnormalities associated with AMD were assigned a grade of. Eyes with extensive intermediate or large (125-µm) drusen were assigned a grade of 3. Eyes with geographic atrophy received a grade of 4. If there was evidence of retinal pigment epithelial detachment or choroidal neovascular membrane, a grade of 5 was assigned. Eyes received a grade of 1 if none of these signs was present. Advanced AMD is defined as grades 4 and 5. To evaluate intergrader reliability, fundus photographs of participants with at least 3 years of follow-up (n=222) were sent to a reading centre for detailed age-related maculopathic grading.

Bibliographic reference	Seddon,Johanna M., Cote,Jennifer, Davis,Nancy, Rosner,Bernard, Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 785-792, 2003
Patient characteristics	Subjects were aged 60 years and older, were primarily white (99.9%), and had at least 1 eye with a best corrected visual acuity of 20/200 or better and non-exudative AMD.
Predictors/risk factors and effect estimates	Risk factors under study include: BMI, Physical activity, smoking, Cardiovascular disease Multivariable analysis was adjusted for: age-sex group (men aged 60-69 years, men aged 70-79 years, men aged 80 years, women aged 60-69 years, women aged 70-79 years, women aged 80 years), education (high school vs high school), smoking (current, past, or never), body mass index (25, 25-29.9, or 30), systolic blood pressure, cardiovascular disease, log energy (continuous), protein intake (quartile), energy-adjusted log beta carotene intake (continuous), alcohol intake (continuous), physical activity (continuous, mean number of times per week of vigorous activity), and initial age-related macular degeneration grade (categorical), total intake of energy-adjusted log zinc, vitamin C, and vitamin E.
Outcomes	Relative Risks for Progression of AMD using measures of BMI, Physical activity, smoking, Cardiovascular disease
Analysis used	Cox proportional hazards model
Length of follow up	Average follow up time was 4.6 years
Missing data handling/loss to follow up	Of the 366 participants enrolled 36 were not considered for analyses because of: Inability to complete the initial study examination (n=5), Lack of follow-up data (n=17), Lack of 1 or more primary independent variables (n=14) Nineteen individuals (7%) were lost to follow-up because of unwillingness to return for additional follow-up examinations. These individuals did not differ significantly from the remaining participants (n=242) with regard to age or education; however, significantly more women were lost to follow-up (10%) compared with men (3%).
Results	Relative risk for progression of AMD from multivariate models including measures of obesity and other risk factors (95% Confidence Intervals) BMI <25: 1.0 (reference) 25-29: 2.32 (1.32-4.07)

Bibliographic reference	Seddon,Johanna M., Cote,Jennifer, Davis,Nancy, Rosner,Bernard, Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 785-792, 2003
	≥30: 2.35 (1.27-4.34) Physical activity (vigorous activity 3 times a week): 0.75 (0.57-1.01) Smoking Never: 1.0 (reference) Past: 1.32 (0.82- 2.12) Current: 1.99 (0.90- 4.43) Cardiovascular disease: No: 1.0 (reference) Yes: 1.21 (0.73-2.02) Adjusted for age-sex group (men aged 60-69 years, men aged 70-79 years, men aged 80 years, women aged 60-69 years, women aged 70-79 years, women aged 80 years), education (high school vs high school), smoking (current, past, or never), body mass index (25, 25-29.9, or 30), systolic blood pressure, cardiovascular disease, log energy (continuous), protein intake (quartile), energy-adjusted log beta carotene intake (continuous), alcohol intake (continuous), physical activity (continuous, mean number of times per week of vigorous activity), and initial age-related macular degeneration grade (categorical), total intake of energy-adjusted log zinc, vitamin C, and vitamin E.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNCLEAR

Bibliographic reference	**Seddon,Johanna M., Cote,Jennifer, Davis,Nancy, Rosner,Bernard, Progression of age-related macular degeneration: association with body mass index, waist circumference, and waist-hip ratio, Archives of ophthalmology (Chicago, Ill.: 1960), 121, 785-792, 2003**
	Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). PARTLY Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Daly,Mark J., Rosner,Bernard, Risk models for progression to advanced age-related macular degeneration using demographic, environmental, genetic, and ocular factors, Ophthalmology, 118, 2203-2211, 2011**
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To expand predictive models for progression to advanced stages of age-related macular degeneration (AMD) based on demographic, environmental, genetic, and ocular factors, using longer follow-up, time varying analyses, calculation of absolute risks, adjustment for competing risks, and detailed baseline AMD and drusen status.
Study dates	Published 2011

Bibliographic reference	**Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Daly,Mark J., Rosner,Bernard, Risk models for progression to advanced age-related macular degeneration using demographic, environmental, genetic, and ocular factors, Ophthalmology, 118, 2203-2211, 2011**
Source of funding	Supported by grants from the National Institutes of Health; the Massachusetts Lions Eye Research Fund Inc; unrestricted grants from Research to Prevent Blindness Inc., New York, NY; the American Macular Degeneration Foundation; Virginia B Smith Fund; and the Age-Related Macular Degeneration Research Fund.
Number of patients	2937 individuals in the Age Related Eye Disease Study
Inclusion Criteria	• Age 55-80 years • At least one eye had to be free from vision-threatening disease other than AMD and cataract • That eye could not have had surgery, except for cataract surgery • The participants' stages of disease ranged from no evidence of AMD in either eye, to advanced AMD with vision loss in one eye but good vision (at least 20/30) in the other eye
Exclusion Criteria	• Non-Caucasian participants
Diagnostic criteria	Based on ocular examination and photographic grading of fundus photographs, participants were defined at baseline as AREDS category 1 in both eyes (essentially free of age-related macular abnormalities), category 2 in the worse eye (mild changes including multiple small drusen, non-extensive intermediate drusen, and/or pigment abnormalities), category 3 in the worse eye (≥1 large drusen of ≥125 micron in diameter, extensive intermediate drusen, and/or non-central GA), category 4 in 1 eye (advanced AMD, either neovascular or central GA, or visual loss owing to AMD regardless of phenotype), or category 4 in both eyes. Because group 3 patients in the original AREDS classification included non-central GA and group 4 included both advanced forms of AMD as well as visual loss regardless of phenotype, we reclassified these groups independent of visual acuity level into grades 4 and 5, with grade 4 including both non-central and central GA, and grade 5 including NV, using the Clinical Age-Related Maculopathy Grading System. Maximum drusen size within the grid (a 3000-micron [μm] radius centred on the fovea) at baseline was used to assess drusen phenotypes for eyes without advanced AMD. Drusen size was based on standard circles with diameters corresponding to 63, 125, and 250 μm. Drusen size was divided into the following categories: <63, 63 to 124, 125 to 249, and ≥250 μm. Progression was defined as either eye progressing from a grade 1, 2, or 3 to either a 4 or a 5 at any follow-up visit to the end of the study within each individual. Time to progression was recorded for the first eye to progress if both eyes were at risk, and for the fellow eye if 1 eye was at risk.

Bibliographic reference	**Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Daly,Mark J., Rosner,Bernard, Risk models for progression to advanced age-related macular degeneration using demographic, environmental, genetic, and ocular factors, Ophthalmology, 118, 2203-2211, 2011**
	Individuals were considered progressors if there was no advanced AMD in either eye at baseline and they developed AMD in ≥1 eye during follow-up (group A), or they had advanced AMD in 1 eye at baseline and progressed to AMD in the fellow eye during follow-up (group B). For subjects in group A, drusen size was controlled for in each eye at baseline and time to progression was evaluated in each eye. The earlier of the 2 progression times was used if both eyes progressed at different times. For subjects in group B, we controlled for AMD category in the affected eye at baseline (i.e., GA or NV), drusen size in the unaffected eye at baseline, and evaluated the time to progression in the fellow eye. Demographic and risk factor data, including education, smoking history, and BMI, were obtained at the baseline visit from questionnaires and height and weight measurements. Antioxidant status was defined as taking antioxidants (antioxidants alone or antioxidants and zinc) or no antioxidants (placebo or zinc alone) in the clinical trial. The clinical trial treatment groups included placebo, antioxidants alone, zinc, and antioxidants plus zinc.
Patient characteristics	Ethnicity: 100% Caucasian
Predictors/risk factors and effect estimates	Variables understudy included: age, gender, education, smoking, body mass index, antioxidants, advanced AMD in 1 eye at baseline, largest drusen size in non-advanced fellow eye, size of drusen in eyes with no advanced AMD at baseline. Models were adjusted for age, sex education, treatment assignment, smoking, BMI, genotypes, drusen phenotypes, and AMD status.
Outcomes	Multivariate Association Between Demographic, Environmental, Genetic and Macular Characteristics and Progression to Advanced Age-Related Macular Degeneration Hazard Ratio (95% CI)
Analysis used	Cox proportional hazards model
Length of follow up	12 years of follow up. The average follow-up time was 9.2 years (range, 0.5–13) for individuals without advanced AMD in either eye at baseline (n = 2519), and was 6.7 years (range, 0.5–12) for subjects who had 1 eye with advanced AMD at baseline (n = 418)

Bibliographic reference	**Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Daly,Mark J., Rosner,Bernard, Risk models for progression to advanced age-related macular degeneration using demographic, environmental, genetic, and ocular factors, Ophthalmology, 118, 2203-2211, 2011**
Missing data handling/loss to follow up	Overall, there were 341 people who were not followed for 5 years and did not progress within 5 years (12%), and 423 people who were not followed for 10 years and did not progress within 10 years (14%). Persons lost to follow-up over 10 years were slightly older (mean age of 69.9 vs 68.5 years), and tended to have better macular status at baseline than subjects who were followed for ≥10 years. There were no differences according to gender or smoking status.
Results	Multivariate Association Between Demographic, Environmental, Genetic and Macular Characteristics and Progression to Advanced Age-Related Macular Degeneration Hazard Ratio (95% CI) **Demographic variables** Age (y) <65: 1.0 65–74: 1.4 (1.1–1.7) ≥75: 1.8 (1.5–2.3) Gender Female: 1.0 Male: 1.0 (0.9–1.2) Education ≤High school: 1.0 >High school: 0.9 (0.8–1.0) **Environmental variables** Smoking Never: 1.0 Past: 1.1 (1.0–1.3) Current: 1.8 (1.4–2.3)

Bibliographic reference	Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Daly,Mark J., Rosner,Bernard, Risk models for progression to advanced age-related macular degeneration using demographic, environmental, genetic, and ocular factors, Ophthalmology, 118, 2203-2211, 2011
	Body mass index (kg/m2) <25: 1.0 25–29: 1.1 (0.9–1.3) ≥30: 1.3 (1.1–1.6) Antioxidants No: 1.0 Yes: 0.9 (0.8–1.0) **Ocular variables** Advanced AMD in 1 eye at baseline Neither eye: 1.0 1 eye with geographic atrophy: 7.3 (2.9–18.4) 1 eye with neovascular disease: 5.1 (2.1–12.2) Largest drusen size (microns) in non-advanced fellow eye <63: 1.0 63–124: 4.1 (1.9–9.2) 125–249: 7.3 (3.4–15.8) ≥250: 11.7 (5.4–25.3) No advanced AMD at baseline: size of drusen (microns) OU <63, <63: 1.0 63–124, <63: 3.5 (1.9–6.3) 63–124, 63–124: 7.6 (4.2–13.5) 125–249,<63: 7.8 (4.1–14.7) 125–249, 63–124: 15.1 (8.8–25.7)

Bibliographic reference	Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Daly,Mark J., Rosner,Bernard, Risk models for progression to advanced age-related macular degeneration using demographic, environmental, genetic, and ocular factors, Ophthalmology, 118, 2203-2211, 2011
	125–249, 125–249: 26.0 (15.4–43.7) ≥ 250, <124: 28.0 (15.2–51.6) ≥ 250, 125–249: 43.9 (26.1–73.9) ≥ 250, ≥250: 53.7 (32.2–89.4)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). PARTLY Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Rosner,Bernard, Validation of a prediction algorithm for progression to advanced macular degeneration subtypes, JAMA ophthalmology, 131, 448-455, 2013
Country/ies where the study was carried out	USA
Study type	2 prospective cohorts
Aim of the study	To develop and validate a predictive model for progression to advanced stages of AMD in 2 independent cohorts.
Study dates	Published 2013 Study cohort based upon people in the Age-Related Eye Disease Study and an independent validation cohort
Source of funding	This work was supported by grants from the National Institutes of Health, the Massachusetts Lions Eye Research Fund Inc, unrestricted grants from Research to Prevent Blindness Inc, the Macula Vision Research Foundation, and the Age-Related Macular Degeneration Research Fund, Ophthalmic Epidemiology and Genetics Service, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts.
Number of patients	AREDs cohort n= 2914 Validation cohort n= 980
Inclusion Criteria	For AREDs study: • Age 55-80 years • At least one eye had to be free from vision-threatening disease other than AMD and cataract • That eye could not have had surgery, except for cataract surgery • The participants' stages of disease ranged from no evidence of AMD in either eye, to advanced AMD with vision loss in one eye but good vision (at least 20/30) in the other eye • For independent validation cohort: unclear • This consisted of white patients (excluding first-degree relatives) who were enrolled in ongoing studies to identify genetic and environmental factors for onset and progression of macular degeneration. Subjects were derived from clinic populations and referrals
Exclusion Criteria	None defined

Bibliographic reference	Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Rosner,Bernard, Validation of a prediction algorithm for progression to advanced macular degeneration subtypes, JAMA ophthalmology, 131, 448-455, 2013
Diagnostic criteria	Participants were classified using the Clinical Age-Related Maculopathy Staging System, based on ocular examination and grading of fundus photographs at baseline, into 5 stages: normal or stage 1 in both eyes (essentially free of age-related macular abnormalities or having only a few small drusen), early AMD or stage 2 in the worse eye (mild changes including multiple small drusen, non-extensive intermediate drusen, and/or pigment abnormalities), intermediate AMD or stage 3 in the worse eye (drusen with a diameter125 m, extensive intermediate drusen), stage 4 in one eye (advanced dry AMD with central or non-central GA), and stage 5 with advanced NV AMD in one eye at baseline. Because category 3 in the original Age-Related Eye Disease Study classification included non-central GA and category 4 included both advanced forms of AMD as well as vision loss regardless of phenotype, we reclassified these groups independent of visual acuity level into Clinical Age-Related Maculopathy Staging System grades 4 (GA) and 5 (NV) as described herein. Progression was defined as either eye progressing from stage 1, 2, or 3 to either stage 4 or stage 5 at any follow-up visit to the end of the study within each individual.
Patient characteristics	**AREDS cohort** (n= 2914) Age, y, n <65: 565 65-74: 1899 ≥75: 450 Sex Female: 1648 Male: 1266 Ethnicity - not described **Validation cohort**

Bibliographic reference	Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Rosner,Bernard, Validation of a prediction algorithm for progression to advanced macular degeneration subtypes, JAMA ophthalmology, 131, 448-455, 2013
	(n= 980) Age, y, n <65: 120 65-74: 383 ≥75: 450: 476 Sex Female: 546 Male: 434 Ethnicity - white patients (excluding first degree relatives)
Predictors/risk factors and effect estimates	Risk factors under study were: Age (<65/65-74/≥75), Sex (Female/Male), Education (≤High school/High school), Smoking (Never/Past/Current), BMI, Genotype.
Outcomes	Hazard ratios for the development of incident advanced age-related macular degeneration:
Analysis used	Cox proportional hazards model
Length of follow up	AREDs: 0.5-13 years (mean 8.8 years) Independent Cohort: 0.10 to 17.9 years (mean, 6.2 years)
Missing data handling/loss to follow up	Unclear/not described
Results	Hazard ratios for the development of incident advanced age-related macular degeneration (95% confidence intervals) *AREDs sample **Validation cohort

Bibliographic reference	Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Rosner,Bernard, Validation of a prediction algorithm for progression to advanced macular degeneration subtypes, JAMA ophthalmology, 131, 448-455, 2013
	Age, y <65: 1 [Reference] 65-74: *1.4 (1.1-1.7) **1.5 (1.0-2.3) ≥75: *2.0 (1.6-2.5) **2.6 (1.7-4.1) Sex Female: 1 [Reference] Male: *1.0 (0.8-1.1) **1.0 (0.8-1.2) Education ≤High school: 1 [Reference] >High school: *0.9 (0.8-1.0) **0.8 (0.6-1.0) Smoking Never: 1 [Reference] Past: *1.2 (1.1-1.4) **1.0 (0.8-1.4) Current: *1.6 (1.3-2.1) **2.2 (1.4-3.3) BMI <25: 1 [Reference] 25-29: *1.1 (0.9-1.3) **1.2 (0.9-1.5) ≥30: *1.3 (1.1-1.6) **1.1 (0.8-1.5) Grade in each eye for individuals without advanced AMD at baseline 1/1, 1/2, or 2/2: *0.09 (0.07-0.1) **0.3 (0.1-0.4) 1/3, 2/3, or 3/3 1 [Reference] 1/4, 2/4, or 3/4 *2.2 (1.6-2.9) **1.4 (0.9-2.1) 1/5, 2/5, or 3/5 *1.2 (1.0-1.4) **1.0 (0.8-1.3)
Limitations	Quality assessment criteria for prognostic studies as outlined in:

Bibliographic reference	**Seddon,Johanna M., Reynolds,Robyn, Yu,Yi, Rosner,Bernard, Validation of a prediction algorithm for progression to advanced macular degeneration subtypes, JAMA ophthalmology, 131, 448-455, 2013**
	Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Seddon,Johanna M., Silver,Rachel E., Kwong,Manlik, Rosner,Bernard, Risk Prediction for Progression of Macular Degeneration: 10 Common and Rare Genetic Variants, Demographic, Environmental, and Macular Covariates, Investigative ophthalmology & visual science, 56, 2192-2202, 2015**
Country/ies where the study was carried out	USA
Study type	Prospective Cohort

Bibliographic reference	**Seddon,Johanna M., Silver,Rachel E., Kwong,Manlik, Rosner,Bernard, Risk Prediction for Progression of Macular Degeneration: 10 Common and Rare Genetic Variants, Demographic, Environmental, and Macular Covariates, Investigative ophthalmology & visual science, 56, 2192-2202, 2015**
Aim of the study	To develop and validate a predictive model for progression to advanced stages of AMD in 2 independent cohorts.
Study dates	Published 2015 Based on data from AREDs study
Source of funding	Supported by Grants from the National Institutes of Health; the Massachusetts Lions Eye Research Fund, Inc.; unrestricted grants from Research to Prevent Blindness, Inc; Foundation Fighting Blindness; the American Macular Degeneration Foundation; and the Age-Related Macular Degeneration Research Fund.
Number of patients	n=2951
Inclusion Criteria	For AREDs study: • Age 55-80 years • At least one eye had to be free from vision-threatening disease other than AMD and cataract • That eye could not have had surgery, except for cataract surgery • The participants' stages of disease ranged from no evidence of AMD in either eye, to advanced AMD with vision loss in one eye but good vision (at least 20/30) in the other eye
Exclusion Criteria	Not described
Diagnostic criteria	Progression was defined as transition from no AMD, early AMD, or intermediate AMD (Clinical Age-Related Maculopathy Staging System [CARMS] grade of 1, 2, or 3) to advanced AMD (CARMS grade 4 or 5) in either eye during a follow-up visit. Progressors were classified using the following two criteria: (1) No advanced AMD was present in either eye at baseline and at least one eye became advanced during follow-up, or (2) advanced AMD was present in one eye at baseline and the fellow eye became advanced during follow-up.
Patient characteristics	AREDs cohort (n= 2914) Age, y, n 54-65: 567 65-74: 1924

Bibliographic reference	**Seddon,Johanna M., Silver,Rachel E., Kwong,Manlik, Rosner,Bernard, Risk Prediction for Progression of Macular Degeneration: 10 Common and Rare Genetic Variants, Demographic, Environmental, and Macular Covariates, Investigative ophthalmology & visual science, 56, 2192-2202, 2015**
	≥75: 460 Sex Female: 1661 Male: 1290 Ethnicity - Caucasian
Predictors/risk factors and effect estimates	Demographic, environmental, and ocular variables understudy in the analyses were age (55–64, 65–74, ‡75), sex, education (high school, >high school), body mass index (BMI) (<25, 25–29, ‡30), smoking status (never, past, current), presence or absence of unilateral advanced AMD at baseline (either central or noncentral geographic atrophy [GA] in one eye [CARMS grade 4] or neovascular disease [NV] in one eye [CARMS grade 5]), and drusen size in eyes without advanced AMD. Drusen size was reported in micrometres for each non-advanced eye as follows: <63, 63 to 124, 125 to 249, and ≥250.
Outcomes	Multivariate Associations Between Baseline Demographic, Environmental, and Macular Variables and Progression to Incident Advanced Age-Related Macular Degeneration (hazard ratios)
Analysis used	Cox proportional hazards Models used individual subjects as the unit of analysis.
Length of follow up	Follow-up time ranged from 6 months to 13 years (mean 8.8 years).
Missing data handling/loss to follow up	For missing demographic or environmental variables, NHANES 2009 data was used to estimate the proportion of subjects with specific levels of education, smoking, and BMI as a function of age–sex groups. Unclear how much information was missing, or loss to follow up.
Results	Multivariate Associations Between Baseline Demographic, Environmental, and Macular Variables and Progression to Incident Advanced Age-Related Macular Degeneration Age, y ≥75: Referent

Bibliographic reference	Seddon,Johanna M., Silver,Rachel E., Kwong,Manlik, Rosner,Bernard, Risk Prediction for Progression of Macular Degeneration: 10 Common and Rare Genetic Variants, Demographic, Environmental, and Macular Covariates, Investigative ophthalmology & visual science, 56, 2192-2202, 2015
	65–74: 0.8 (0.6–0.9) 55–64: 0.6 (0.5–0.7) Sex Female: Referent Male: 1.1 (0.9–1.2) Education High school: Referent >High school: 0.9 (0.8–1.0) Smoking Never: Referent Past: 1.1 (1.0–1.3) Current: 1.8 (1.4–2.3) BMI <25: Referent 25–29: 1.1 (0.9–1.3) ≥30: 1.2 (1.0–1.5) Advanced AMD Neither eye: Referent Grade 4: 8.3 (3.2–19.9) Grade 5: 5.8 (2.3–13.2) Advanced AMD in one eye: largest drusen size in non-advanced eye, μm None to <63: Referent 63–124: 3.9 (1.7–8.6)

Bibliographic reference	Seddon,Johanna M., Silver,Rachel E., Kwong,Manlik, Rosner,Bernard, Risk Prediction for Progression of Macular Degeneration: 10 Common and Rare Genetic Variants, Demographic, Environmental, and Macular Covariates, Investigative ophthalmology & visual science, 56, 2192-2202, 2015
	125–249: 8.4 (3.9–18.3) ≥250: 13.8 (6.4–29.5) No advanced AMD: largest drusen size in each eye, µm None to <63, none to <63: Referent 63–124, none to <63: 3.0 (1.7–5.3) 63–124, 63–124: 7.9 (4.5–13.8) 125–249, none to <63: 7.2 (3.9–13.3) 125–249, 63–124: 15.2 (9.1–25.2) 125–249, 125–249: 29.0 (17.7–47.5) ‡250, ≤124: 31.0 (17.2–55.9) ‡250, 125–249: 50.3 (30.8–82.2) ‡250, ≥250: 72.0 (44.7–116.2) Hazard ratios are adjusted for all variables in table and the four AREDS treatment groups.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). UNSURE

Bibliographic reference	**Seddon,Johanna M., Silver,Rachel E., Kwong,Manlik, Rosner,Bernard, Risk Prediction for Progression of Macular Degeneration: 10 Common and Rare Genetic Variants, Demographic, Environmental, and Macular Covariates, Investigative ophthalmology & visual science, 56, 2192-2202, 2015**
	Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). UNSURE Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Submacular Surgery Trials Research Group, Solomon,S.D., Jefferys,J.L., Hawkins,B.S., Bressler,N.M., Bressler,S.B., 20091202, Risk factors for second eye progression to advanced age-related macular degeneration: SST report No. 21 Submacular Surgery Trials Research Group, Retina (Philadelphia, Pa.)Retina, 29, 1080-1090, 2009**
Country/ies where the study was carried out	USA
Study type	Prospective cohort
Aim of the study	To identify characteristics predictive of progression to advanced age-related macular degeneration (AMD) in second (fellow) eyes of participants in the Submacular Surgery Trials (SST) who had unilateral neovascular AMD at study entry.
Study dates	Published 2009
Source of funding	Sponsored by the National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Sciences.
Number of patients	370 fellow eyes of participants in the submacular surgery trials who had a unilateral neovascular AMD at study entry.
Inclusion Criteria	• From the two submacular surgery trials • Confirmed to be at risk of choroidal neovascularisation or foveal geographical atrophy in the second eye (advanced AMD)
Exclusion Criteria	• Choroidal neovascularisation or foveal geographical atrophy in the second eye (advanced AMD) at baseline

Bibliographic reference	**Submacular Surgery Trials Research Group, Solomon,S.D., Jefferys,J.L., Hawkins,B.S., Bressler,N.M., Bressler,S.B., 20091202, Risk factors for second eye progression to advanced age-related macular degeneration: SST report No. 21 Submacular Surgery Trials Research Group, Retina (Philadelphia, Pa.)Retina, 29, 1080-1090, 2009**
Diagnostic criteria	Baseline stereoscopic film-based colour photographs of the fellow eye of participants with a second eye at risk of progression to choroidal neovascularisation or focal geographic atrophy were re-evaluated by two trained and experienced Wilmer Reading Centre graders who were masked as to the presenting clinical features and subsequent course. Each grader provided an independent assessment utilizing a system that was largely adapted from the AREDS criteria for classifying features of AMD. Key examination tools of the AREDS system were a set of standard and example photographs, a standard transparent grid overlay, and graduated measurement circles.
Patient characteristics	Total (n=370) Age, years <75: 37% 75-79: 31% ≥80: 33% Gender Women: 49% Male: 51%
Predictors/risk factors and effect estimates	Risk factors under study included: non-foveal geographic atrophy, nongeographic atrophy, focal hyperpigmentation, maximum drusen size and maximum drusen area. Other covariates adjusted for were: gender, age, smoking, hypertension history, predominant lesion component in the first eye, visual acuity of the eye at risk.
Outcomes	Multivariate analysis of risk of advanced AMD of ocular factors in the study eye, Hazard ratios (95% confidence intervals) Multivariate analysis of risk of advanced AMD, of ocular factors in the fellow eye, Hazard ratios (95% confidence intervals)
Analysis used	Cox proportional hazards model
Length of follow up	Up to 4 years

Bibliographic reference	**Submacular Surgery Trials Research Group, Solomon,S.D., Jefferys,J.L., Hawkins,B.S., Bressler,N.M., Bressler,S.B., 20091202, Risk factors for second eye progression to advanced age-related macular degeneration: SST report No. 21 Submacular Surgery Trials Research Group, Retina (Philadelphia, Pa.)Retina, 29, 1080-1090, 2009**
Missing data handling/loss to follow up	Loss to follow up/missing data not described
Results	Multivariate analysis of risk of advanced AMD of ocular factors in the study eye, Hazard ratios (95% confidence intervals) Drusen <250 µm in diameter: 1.00 (referent) Drusen ≥250 µm in diameter: 1.73 (1.12-2.66) No focal hyperpigmentation: 1.00 Mild/moderate focal hyperpigmentation: 1.43 (0.86-2.40) Severe focal hyperpigmentation: 2.26 (1.30-3.94) No geographic atrophy: 1.00 (referent) Geographic atrophy that spares the foveal centre: 1.82 (1.08-3.08) Multivariate analysis of risk of advanced AMD, of ocular factors in the fellow eye, Hazard ratios (95% confidence intervals) Drusen <250 µm in diameter in the fellow eye: 1.00 (referent) Drusen ≥250 µm in diameter in the fellow eye: 2.32 (1.49-3.61) Nongeographic atrophy (retinal pigment epithelium depigmentation) not present in the fellow eye: 1.00 (referent) Nongeographic atrophy (retinal pigment epithelium depigmentation) present in the fellow eye: 1.79 (1.14-2.82) Cox proportional hazard model was adjusted for gender, age, smoking, hypertension history, predominant lesion component in the first eye, visual acuity of the eye at risk. Non-significant factors included: maximum drusen area
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors

Bibliographic reference	**Submacular Surgery Trials Research Group, Solomon,S.D., Jefferys,J.L., Hawkins,B.S., Bressler,N.M., Bressler,S.B., 20091202, Risk factors for second eye progression to advanced age-related macular degeneration: SST report No. 21 Submacular Surgery Trials Research Group, Retina (Philadelphia, Pa.)Retina, 29, 1080-1090, 2009**
	Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**van,Leeuwen R., Boekhoorn,S., Vingerling,J.R., Witteman,J.C., Klaver,C.C., Hofman,A., de Jong,P.T., 20051230, Dietary intake of antioxidants and risk of age-related macular degeneration, JAMA, 294, 3101-3107, 2005**
Country/ies where the study was carried out	Netherlands, Rotterdam study
Study type	Prospective cohort study

Bibliographic reference	van,Leeuwen R., Boekhoorn,S., Vingerling,J.R., Witteman,J.C., Klaver,C.C., Hofman,A., de Jong,P.T., 20051230, Dietary intake of antioxidants and risk of age-related macular degeneration, JAMA, 294, 3101-3107, 2005
Aim of the study	To investigate whether regular dietary intake of antioxidants is associated with a lower risk of incident AMD.
Study dates	Published 2005 Data collected 1990- 1993
Source of funding	This study was supported by unrestricted grants from the following organizations: Netherlands Organization for Scientific Research, the Hague; Optimix, Amsterdam; Physico Therapeutic Institute, Rotterdam; Blindenpenning, Amsterdam; Sint Laurens Institute, Rotterdam; Bevordering van Volkskracht, Rotterdam; Blindenhulp, the Hague; Rotterdamse Blindenbelangen Association, Rotterdam; Oogheelkundige Ondersteuning, the Hague; kfHein, Utrecht; Ooglijders, Rotterdam; Prins Bernhard Cultuurfonds, Amsterdam; Van Leeuwen Van Lignac, Rotterdam; Verhagen, Rotterdam; General Netherlands Society for the Prevention of Blindness, Doorn; Landelijke Stichting voor Blinden en Slechtzienden, Utrecht; and Elise Mathilde, Maarn. An unrestricted grant was obtained from Topcon Europe BV, Capelle aan de IJssel.
Number of patients	5836 persons at risk of AMD 4765 had reliable dietary data and 4170 participated in the follow up
Inclusion Criteria	• Population-based cohort of all inhabitants aged 55 years or older in a middleclass suburb of Rotterdam. • No AMD in either eye at baseline; i.e. with no drusen or pigment irregularities, hard drusen only, or soft drusen without pigment irregularities.
Exclusion Criteria	• Participants with decreased cognitive function (defined as a score 80 on the Cambridge Examination of Mental Disorders in the Elderly) • Nursing home residents because their food was prepared by nursing home staff and would not reflect past dietary habits. • Logical inconsistencies in dietary interviews, missing the baseline dietitian visit when the food frequency questionnaire was administered, or various other logistical reasons
Diagnostic criteria	The eye examination included 35° fundus photography. Two experienced graders, masked to dietary intake, graded the follow-up transparencies and afterward compared these with the baseline ones. The grading procedures, definitions, and graders were identical at baseline and follow-up. Early-stage AMD was defined as the presence of either large (63 µm), soft, distinct drusen with pigment irregularities or indistinct (125 µm) or reticular drusen with or without pigment irregularities.

Bibliographic reference	van,Leeuwen R., Boekhoorn,S., Vingerling,J.R., Witteman,J.C., Klaver,C.C., Hofman,A., de Jong,P.T., 20051230, Dietary intake of antioxidants and risk of age-related macular degeneration, JAMA, 294, 3101-3107, 2005
	Late-stage AMD, mostly leading to blindness, was defined as geographic atrophy (both central and noncentral), choroidal neovascularization, or a combination of both. At baseline, participants completed a checklist at home that queried foods and drinks they had consumed at least twice a month during the preceding year as well as dietary habits, use of supplements, and prescribed diets. Next, during their visit to the research centre, they underwent a standardized interview with a dietitian based on the checklist, using a 170-item semi-quantitative food frequency questionnaire
Patient characteristics	Baseline Characteristics: *Incident Age-Related Macular Degeneration at follow up (n = 560), **No Age-Related Macular Degeneration at Follow-up (n = 3610) Age, y, mean (SD) *68.2 (7.1) **66.4 (7.2) Women, No. (%) *321 (57.3) **2151 (59.6) Ethnicity: not described
Predictors/risk factors and effect estimates	Risk factors under study: Total energy intake and nutrient intake per day with the computerized Dutch Food Composition Table: carotenoids alpha and beta carotene, beta cryptoxanthin, lutein/zeaxanthin, lycopene, vitamins A (retinol equivalents), C, and E, and iron and zinc as cofactors for antioxidant enzymes. People who reported taking supplements containing carotenoids, vitamins A, C, or E, iron, or zinc, as well as multivitamins or multiminerals, were classified as supplement users. Confounders included in analysis: Smoking status (current, former, or never, and number of pack-years), Serum total cholesterol level, Blood pressure, ankle-arm index, carotid intimamedia thickness and atherosclerotic plaques, subclinical atherosclerosis composite.
Outcomes	Risk of Age-Related Macular Degeneration per Standard Deviation (SD) Increase in Dietary Intake of Antioxidant Nutrients. Risk of Age-Related Macular Degeneration by Category of Combined Intake of 4 Predefined Antioxidant Nutrients (Vitamins C and E, Beta Carotene, and Zinc).

Bibliographic reference	van,Leeuwen R., Boekhoorn,S., Vingerling,J.R., Witteman,J.C., Klaver,C.C., Hofman,A., de Jong,P.T., 20051230, Dietary intake of antioxidants and risk of age-related macular degeneration, JAMA, 294, 3101-3107, 2005
Analysis used	Cox proportional hazards regression analysis
Length of follow up	Mean follow-up of 8.0 years (range, 0.3-13.9 years).
Missing data handling/loss to follow up	Analysis: Dietary intake was not assessed in 227 participants with decreased cognitive function (defined as a score 80 on the Cambridge Examination of Mental Disorders in the Elderly) because their dietary history was deemed unreliable. Also excluded were 179 nursing home residents because their food was prepared by nursing home staff and would not reflect past dietary habits. Reliable dietary data were missing in 665 participants because of logical inconsistencies in dietary interviews, missing the baseline dietitian visit when the food frequency questionnaire was administered, or various other logistical reasons. Baseline characteristics were similar in the 2 groups, although eligible respondents without dietary data were, on average, somewhat older compared with those with data and included fewer women. Follow up: Of the baseline cohort, 156 participants died, 419 refused any follow-up examination, and 20 were lost to follow-up before the first follow-up examination. Nonparticipants tended to be older; included more women, nursing home residents, and smokers; and more often had systemic hypertension. They did not differ from participants in their dietary intake of antioxidants;
Results	Risk of Age-Related Macular Degeneration per Standard Deviation (SD) Increase in Dietary Intake of Antioxidant Nutrients. Hazard ratios (95% confidence intervals) Carotenoids Alpha carotene 0.99 (0.94-1.06) Beta carotene: 1.00 (0.94-1.06) Beta cryptoxanthin: 1.01 (0.92-1.10) Lutein/zeaxanthin: 1.01 (0.93-1.09) Lycopene: 1.01 (0.97-1.04) Vitamins

Bibliographic reference	van,Leeuwen R., Boekhoorn,S., Vingerling,J.R., Witteman,J.C., Klaver,C.C., Hofman,A., de Jong,P.T., 20051230, Dietary intake of antioxidants and risk of age-related macular degeneration, JAMA, 294, 3101-3107, 2005
	Vitamin A (retinol equivalents): 0.95 (0.86-1.05) Vitamin C: 1.02 (0.94-1.10) Vitamin E: 0.92 (0.84-1.00) Trace elements Iron: 0.95 (0.86-1.04) Zinc: 0.91 (0.83-0.98) Hazard ratios were adjusted for age, sex, body-mass index, smoking status, pack-years of smoking, systolic blood pressure, atherosclerosis composite score, serum total cholesterol, and alcohol intake. Risk of Age-Related Macular Degeneration by Category of Combined Intake of 4 Predefined Antioxidant Nutrients (Vitamins C and E, Beta Carotene, and Zinc). Low: 1.20 (0.92-1.56) Medium: 1.00 (referent) High: 0.65 (0.46-0.92) Categories were defined by using the median energy-adjusted daily intake per nutrient as a cutoff value and classifying above-median intake of all nutrients as high intake and below-median intake of all nutrients as low intake. Cutoff values were 114 mg for vitamin C, 13 mg for vitamin E, 3.6 mg for beta carotene, and 9.6 mg for zinc. Hazard ratios were adjusted for age, sex, body mass index, smoking status, pack-years of smoking, systolic blood pressure, atherosclerosis composite score, serum total cholesterol, and alcohol intake.
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE

Bibliographic reference	van,Leeuwen R., Boekhoorn,S., Vingerling,J.R., Witteman,J.C., Klaver,C.C., Hofman,A., de Jong,P.T., 20051230, Dietary intake of antioxidants and risk of age-related macular degeneration, JAMA, 294, 3101-3107, 2005
	Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). NO Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). YES Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). YES The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	VanderBeek,Brian L., Zacks,David N., Talwar,Nidhi, Nan,Bin, Musch,David C., Stein,Joshua D., Racial differences in age-related macular degeneration rates in the United States: a longitudinal analysis of a managed care network, American journal of ophthalmology, 152, 273-282, 2011
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To investigate the association between race and the development of AMD in the USA population
Study dates	From January 1, 2001 through December 31, 2007
Source of funding	Grant support from National Eye Institute K23 Mentored Clinician Scientist Award (JDS; EY019511), Blue Cross Blue Shield of Michigan Foundation (JDS), an unrestricted grant from Research to Prevent Blindness, Research to Prevent Blindness

Bibliographic reference	**VanderBeek,Brian L., Zacks,David N., Talwar,Nidhi, Nan,Bin, Musch,David C., Stein,Joshua D., Racial differences in age-related macular degeneration rates in the United States: a longitudinal analysis of a managed care network, American journal of ophthalmology, 152, 273-282, 2011**
	Lew R. Wasserman Merit Award (DCM), Research to Prevent Blindness Sybil B. Harrington Special Scholar Award for Macular Degeneration (DNZ).
Number of patients	2,259,061 individuals in the medical plan who met the inclusion criteria, 1,772,962 individuals (79%) were able to be classified according to race. There were 1,535,008 whites (87%), 78,315 blacks (4%), 99,518 Latinos (6%), and 44,103 Asian Americans (3%).
Inclusion Criteria	• This study only included patients insured through one specific managed care network
Exclusion Criteria	• Non-continuous enrolment in a medical plan • Enrolment in a medical plan up to one year • Individuals with duplicate or erroneous data • Enrolees without one or more CPT codes indicating a visit to an ophthalmologist or optometrist • Having received a prior diagnosis of AMD
Diagnostic criteria	All individuals age 40 or older who were in the i3 InVision Data Mart database for more than one consecutive year and had one or more visits to an eye care provider during their time in the medical plan were identified. The race of each beneficiary was identified by the managed care company using information provided from two sources: public records (driver's license data) and from E-Tech (Ethnic Technologies, LLC., South Hackensack, NJ), a tool that uses information from the name of the beneficiary and the census block he or she lives in to assign race. Races were categorized as non-Hispanic white (referred to as white), black, Latino, and Asian American. All other races were categorized as "Other". ICD-9CM codes were used to determine whether each beneficiary had one or more diagnoses of AMD during their time in the medical plan. Incidence and prevalence rates were determined for non-exudative AMD and exudative AMD.
Patient characteristics	Age: The median age at entry into the plan was 52 years (range 40–87 years) Gender: overall gender break down of sample not provided Ethnicity: There were 1,535,008 whites (87%), 78,315 blacks (4%), 99,518 Latinos (6%), and 44,103 Asian Americans (3%).
Predictors/risk factors and effect estimates	Risk factors of interest included: Ethnicity: Black, Latino, Asian American, White

Bibliographic reference	**VanderBeek,Brian L., Zacks,David N., Talwar,Nidhi, Nan,Bin, Musch,David C., Stein,Joshua D., Racial differences in age-related macular degeneration rates in the United States: a longitudinal analysis of a managed care network, American journal of ophthalmology, 152, 273-282, 2011**
	Analysis was adjusted for: age, sex, household net worth, education level, geographic region of residence within the US, systemic hypertension, skin cancer, anaemia, heart disease, myocardial infarction, stroke, peripheral vascular disease, renal disease, systemic hypotension, obesity, diabetes mellitus, hyperlipidaemia, coagulopathies, open-angle glaucoma, cataract, pseudophakia / aphakia, and diabetic retinopathy.
Outcomes	Multivariable adjusted hazard of developing non-exudative or exudative AMD stratified by race and age (compared to white populations at similar ages)
Analysis used	Cox regression analysis
Length of follow up	Average enrolment time within the plan was 3.75 ± 1.81 years. Persons were followed one year after enrolment until they either were diagnosed with the condition (non-exudative or exudative AMD) or were censored (either when they left the medical plan or the last day for which we had data, December 31, 2007)
Missing data handling/loss to follow up	No information regarding missing data was provided. Participants with erroneous data were excluded.
Results	Multivariable adjusted hazard of developing non-exudative or exudative AMD stratified by race and age (compared to white populations at similar ages) (95% confidence intervals): Whites at similar age= referent Blacks at age 60: Non-exudative AMD: 0.75 (0.71-0.79) Exudative AMD: 0.70 (0.59-0.83) Blacks at age 80 Non-exudative AMD: 0.56 (0.52-0.60) Exudative AMD: 0.45 (0.37-0.54)

Bibliographic reference	**VanderBeek,Brian L., Zacks,David N., Talwar,Nidhi, Nan,Bin, Musch,David C., Stein,Joshua D., Racial differences in age-related macular degeneration rates in the United States: a longitudinal analysis of a managed care network, American journal of ophthalmology, 152, 273-282, 2011**
	Latinos at age 60 Non-exudative AMD: 0.99 (0.94-1.04) Exudative AMD: 1.28 (1.13-1.45) Latinos at age 80 Non-exudative AMD: 0.82 (0.76-0.88) Exudative AMD: 0.89 (0.76-1.05) Asian Americans at age 60 Non-exudative AMD: 1.28 (1.20-1.36) Exudative AMD: 1.08 (0.89-1.31) Asian Americans at age 80 Non-exudative AMD: 0.92 (0.83-1.02) Exudative AMD: 0.54 (0.40-0.73)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE

Bibliographic reference	VanderBeek,Brian L., Zacks,David N., Talwar,Nidhi, Nan,Bin, Musch,David C., Stein,Joshua D., Racial differences in age-related macular degeneration rates in the United States: a longitudinal analysis of a managed care network, American journal of ophthalmology, 152, 273-282, 2011
	Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). NO Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	Williams,P.T., 20090116, Prospective study of incident age-related macular degeneration in relation to vigorous physical activity during a 7-year follow-up, Investigative ophthalmology & visual science, 50, 101-106, 2009
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To test whether the risk of age-related macular degeneration (AMD) decreases with vigorous physical activity.
Study dates	Published 2009 Recruiting between 1991 and 1993
Source of funding	Unclear
Number of patients	Male (n=29,532) and female (n=12,176)
Inclusion Criteria	National Runners Health Study: Cohort of runners, 18 years old and older, was recruited between 1991 and 1993 by distributing a two-page questionnaire nationally to runners identified through subscription lists to running magazines and among participants of foot race events.

Bibliographic reference	**Williams,P.T., 20090116, Prospective study of incident age-related macular degeneration in relation to vigorous physical activity during a 7-year follow-up, Investigative ophthalmology & visual science, 50, 101-106, 2009**
Exclusion Criteria	• Subjects reporting being diagnosed in the same year as their baseline survey or before were excluded from the analyses. • Subjects who were diabetic at baseline were excluded from all analyses.
Diagnostic criteria	Participants reported whether they had received a clinical diagnosis of macular degeneration since their baseline questionnaire and provided the year of diagnosis. The questionnaire solicited information on demographics, running history, weight history, smoking habits, prior history of heart attacks and cancer, and medications for blood pressure, thyroid, cholesterol, and diabetes. Running distances were reported in usual miles run per week at baseline. BMI was calculated as self-reported weight in kilograms divided by the square of self-reported height in meters. Self-reported waist circumferences were elicited by the question, “Please provide, to the best of your ability, your body circumference in inches.” without further instruction. Intakes of meat, fish, and fruit were based on the questions: “During an average week, how many servings of beef, lamb, or pork do you eat,” “...servings of fish do you eat,” and “...pieces of fruit do you eat?” Alcohol intake was estimated from the corresponding questions for 4-oz. (112 mL) glasses of wine, 12-oz. (336 mL) bottles of beer, and mixed drinks and liqueurs. Alcohol was computed as 10.8 g per 4-oz glass of wine, 13.2 g per 12 oz. bottle of beer, and 15.1 g per mixed drink. For this report, baseline cardiorespiratory fitness was defined as speed in meters per second of the participant’s best time in a 10-km race during the previous 5 years (reported as finishing time in minutes).
Patient characteristics	Incident AMD: *Present (n=152), **Absent Present Absent (41,556) Female (%): *27.63 **29.20 Age (y), mean and standard deviation: *54.22 ± 0.92 **43.09 ± 0.05*
Predictors/risk factors and effect estimates	The dose–response relationships of incident AMD to baseline running distance, cardiorespiratory fitness, body weight, and circumferences was under study. Models were adjusted for: Reported weekly intakes of alcohol, meat, fish, and fruit, age, and BMI when analysing physical activity.
Outcomes	Relative Risk for AMD with Physical Activity (km/day) Relative Risk for AMD with Cardiorespiratory Fitness (m/s)
Analysis used	Cox proportional hazards analyses

Bibliographic reference	Williams,P.T., 20090116, Prospective study of incident age-related macular degeneration in relation to vigorous physical activity during a 7-year follow-up, Investigative ophthalmology & visual science, 50, 101-106, 2009
Length of follow up	7 year follow up
Missing data handling/loss to follow up	Approximately 15% returned baseline questionnaires among the total original eligible number contacted (the exact number is not known because of uncertainty of the number actually distributed and the proportion of subjects who receive duplicate questionnaires). Eighty percent of the original cohort, who provided baseline questionnaires provided follow-up surveys to us 7 years later or were known dead.
Results	Relative Risk for AMD, Physical Activity (km/day) (95% confidence intervals) 0.90 (0.83-0.97) Relative Risk for AMD, Cardiorespiratory Fitness (m/s) (95% confidence intervals) 0.92 (0.60-1.39)* *34,035 men and women provided 10-km performance times (to calculate cardiorespiratory fitness).
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). NO Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO

Bibliographic reference	**Williams,P.T., 20090116, Prospective study of incident age-related macular degeneration in relation to vigorous physical activity during a 7-year follow-up, Investigative ophthalmology & visual science, 50, 101-106, 2009**
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES

Bibliographic reference	**Wilson,H.L., Schwartz,D.M., Bhatt,H.R., McCulloch,C.E., Duncan,J.L., 20040427, Statin and aspirin therapy are associated with decreased rates of choroidal neovascularization among patients with age-related macular degeneration, American journal of ophthalmology, 137, 615-624, 2004**
Country/ies where the study was carried out	USA
Study type	Retrospective cohort study of people with AMD
Aim of the study	To find the association between statin or aspirin therapy and the development of choroidal neovascularisation
Study dates	January 1 1990 to March 1 2003
Source of funding	Career development award from Research to Prevent Blindness and grants from the National Eye Institute and That Man May See, Inc. and The Foundation for Fighting Blindness
Number of patients	326 patients with AMD, 104 with CNV, 204 with dry AMD and 18 with Geographic atrophy.
Inclusion Criteria	• 60 years or older • Diagnosed with AMD • Followed in the SFVA eye and medical practice during the study period
Exclusion Criteria	• Ocular diseases other than AMD that are associated with CNV, • Younger than 60 years old • Not enrolled in the medical practice clinic or with incomplete medication data in the medical records, • Treated with statins for less than 6 months.

Bibliographic reference	**Wilson,H.L., Schwartz,D.M., Bhatt,H.R., McCulloch,C.E., Duncan,J.L., 20040427, Statin and aspirin therapy are associated with decreased rates of choroidal neovascularization among patients with age-related macular degeneration, American journal of ophthalmology, 137, 615-624, 2004**
Diagnostic criteria	All eye photography files were reviewed by a retina specialist (D.M.S. or J.L.D.) masked to the subject's medical record and classified as having either non-neovascular AMD or angiographically evident choroidal neovascularization (CNV), according to standard definitions of non-neovascular and neovascular AMD based on fundus photographic and angiographic characteristics. Fundus photographs of subjects with non-neovascular (dry) AMD showed at least five soft indistinct drusen with or without retinal pigment epithelial abnormalities within the macula in each eye. In addition to these findings, subjects with dry AMD and geographic atrophy (GA) also showed a discrete area of retinal depigmentation, at least 175 m in diameter, with a sharp border and visible choroidal vessels with no evidence of CNV.9 Subjects with dry AMD were required to have a dilated funduscopic examination including biomicroscopy in the medical record confirming the absence of CNV. Fundus photographs of subjects with CNV showed drusen and/or retinal pigment epithelial changes in at least one eye, in addition to CNV evidenced by subretinal macular haemorrhage, lipid deposits in the macula, fibrotic macular scarring, or retinal pigment epithelial detachment on fundus photographs. All CNV subjects had angiographic evidence of CNV or a clinic note documenting a disciform scar with prior photos demonstrating drusen.
Patient characteristics	Baseline characteristics: Median Age (range): CNV- 75 (61-93) Early AMD- 77 (60-97) Geographic atrophy- 78 (61-91) Ethnicity White (percentage) CNV- 84 Early AMD- 75 Geographic atrophy- 94 Men (%) CNV- 95

Bibliographic reference	**Wilson,H.L., Schwartz,D.M., Bhatt,H.R., McCulloch,C.E., Duncan,J.L., 20040427, Statin and aspirin therapy are associated with decreased rates of choroidal neovascularization among patients with age-related macular degeneration, American journal of ophthalmology, 137, 615-624, 2004**
	Early AMD- 95 Geographic atrophy- 94 All of the above entered into multivariable analysis
Predictors/risk factors and effect estimates	Variables associated with disease status (P.05) were tested in a multi-predictor model, along with possible confounding variables that might be associated with statin use, aspirin use, or CNV, including hypertension; antihypertensive medication use; coronary artery disease; family history of coronary artery disease; prior myocardial infarction; prior stroke; prior Hollenhorst plaques; diabetes; and baseline serum total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein cholesterol, and triglycerides to test for the independent effects of the variables.
Outcomes	Significant variables associated with the risk of developing CNV in a person with AMD Reported as hazard ratios
Analysis used	Because observation times were unequal, a parametric, interval censored data regression was performed on age of onset of CNV using Proc LIFEREG in SAS for Windows version 9 (SAS Institute, Inc., Cary, North Carolina, USA) assuming a Weibull distribution. A sensitivity analysis was performed and a probability plot generated to check the Weibull parametric assumption. Predictors were eliminated sequentially on the basis of statistically insignificant tests based on Wald 2 statistics.
Length of follow up	Retrospective data collected over 13 years
Missing data handling/loss to follow up	Because observation times were unequal, parametric, interval censored data regression was performed. Retrospective therefore no loss to follow up.
Results	Hazard ratios (95% Confidence interval): Current smoker: 1.77 (1.06-2.97) Aspirin user: 0.63 (0.40- 0.98) Non-significant factors of interest on the univariate level: Ethnicity, Gender, Age, Hypertension, history of MI, Diabetes, history of CVA (cerebrovascular accident) or TIA (transient ischaemic attack), Coronary artery disease.

Bibliographic reference	**Wilson,H.L., Schwartz,D.M., Bhatt,H.R., McCulloch,C.E., Duncan,J.L., 20040427, Statin and aspirin therapy are associated with decreased rates of choroidal neovascularization among patients with age-related macular degeneration, American journal of ophthalmology, 137, 615-624, 2004**
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). YES Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). YES Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). PARTLY Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis) YES

Bibliographic reference	**Stein,Joshua D., VanderBeek,Brian L., Talwar,Nidhi, Nan,Bin, Musch,David C., Zacks,David N., Rates of nonexudative and exudative age-related macular degeneration among Asian American ethnic groups, Investigative ophthalmology & visual science, 52, 6842-6848, 2011**
Country/ies where the study was carried out	USA
Study type	Prospective cohort study
Aim of the study	To determine whether the risk for non-exudative and exudative age-related macular degeneration (AMD) varies for Americans of different Asian ethnicities.
Study dates	From January 1, 2001 through December 31, 2007
Source of funding	Grant support from National Eye Institute K23 Mentored Clinician Scientist Award (JDS; EY019511), Blue Cross Blue Shield of Michigan Foundation (JDS), an unrestricted grant from Research to Prevent Blindness, Research to Prevent Blindness Lew R. Wasserman Merit Award (DCM), Research to Prevent Blindness Sybil B. Harrington Special Scholar Award for Macular Degeneration (DNZ).
Number of patients	44,103 Asian Americans
Inclusion Criteria	• This study only included patients insured through one specific US managed care network • All persons aged 40 and older who had >=1 visit to an eye care provider and were in the database for >=1 consecutive year
Exclusion Criteria	• Non-continuous enrolment in a medical plan • Enrolment in a medical plan up to one year • Individuals with duplicate or erroneous data • Enrolees without one or more CPT codes indicating a visit to an ophthalmologist or optometrist • Having received a prior diagnosis of AMD
Diagnostic criteria	ICD-9CM codes were used to determine whether each beneficiary had 1 diagnosis of non-exudative AMD (ICD-9CM codes 362.50, 362.51, and 362.57) or exudative AMD (362.52) during their time in the medical plan. Incidence and prevalence rates were determined for both AMD types. Each enrolee could have more than one form of AMD during their time in the plan. Two sources were used by the managed care company to identify race and ethnicity: public records (driver's license data) and E-Tech (Ethnic Technologies, South Hackensack, NJ), a tool that uses information from the beneficiary name and the census block to assign race and ethnicity. Previous comparisons between information collected by patient self-report and

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	assignment of race using E-Tech demonstrated that E-Tech has a positive predictive value of 71%, and information from the company indicates this software actually has a 96% accuracy at correctly classifying patients based on race and ethnicity. Patients of Asian American descent were identified, and each was classified by ethnicity: Chinese, Filipino, Indian, Japanese, Korean, Pakistani, and Vietnamese. There were inadequate numbers of Bangladeshis, Burmese, Laotians, Thais, Indonesians, Malaysians, Hawaiians, Samoans, and Sri Lankans to study these groups separately. Those of these ethnicities were classified as “other.”
Patient characteristics	Age: The median age at entry into the plan was 52 years (range 40–87 years), for white Americans, the median age was 52 years; for Asian Americans it was 50 years. Gender: overall gender break down of sample not provided Ethnicity: Overall sample, n= 225,9061 Non-Asian Whites 1,535,008 Vietnamese 5,420 228 Japanese 4,771 Chinese 15,918 Filipino 2,514 Korean 3,948 Indian 8,312 Pakistani 1,000 Other Asian 2,220
Predictors/risk factors and effect estimates	Risk factors of interest included: Ethnicity: Vietnamese, Japanese, Chinese, Filipino, Korean, Indian, Pakistani Analysis was adjusted for:

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	Multivariable analyses were adjusted for age, sex, region of residence within the United States, education level, household net worth, diabetes mellitus, hypertension, hyperlipidaemia, obesity, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident, renal insufficiency, coagulopathy, blood-loss anaemia, deficiency anaemias, systemic, hypotension, skin cancer, cataract, pseudophakia or aphakia, diabetic retinopathy, and open-angle glaucoma.
Outcomes	Multivariable adjusted hazard of developing non-exudative or exudative AMD stratified by race and cge (compared to white populations at similar ages)
Analysis used	Cox regression analysis
Length of follow up	Not all participants were in the plan for the full 7 years. Incidence rates of non-exudative and exudative AMD were calculated by dividing the number of newly diagnosed beneficiaries with each AMD type by their time, in person-years, in the plan at risk.
Missing data handling/loss to follow up	No information regarding missing data was provided. Participants with erroneous data were excluded.
Results	Hazard ratios for the risk of non-exudative AMD (95% confidence intervals) Reference group - white Americans Vietnamese: 1.15 (0.96–1.38) Japanese: 0.71 (0.59–0.85) Chinese: 1.63 (1.50–1.77) Filipino: 0.96 (0.76–1.22) Korean: 1.11 (0.92–1.34) Indian: 0.99 (0.85–1.16) Pakistani: 1.97 (1.40–2.77) Hazard ratios for the risk of exudative AMD (95% confidence intervals)

Bibliographic reference	**Stein,Joshua D., VanderBeek,Brian L., Talwar,Nidhi, Nan,Bin, Musch,David C., Zacks,David N., Rates of nonexudative and exudative age-related macular degeneration among Asian American ethnic groups, Investigative ophthalmology & visual science, 52, 6842-6848, 2011**
	Reference group - white Americans Vietnamese: 0.70 (0.37–1.35) Japanese: 0.64 (0.40–1.04) Chinese: 0.95 (0.71–1.27) Filipino: 1.18 (0.67–2.09) Korean: 0.97 (0.56–1.66) Indian: 1.08 (0.71–1.62) Pakistani: 0.45 (0.06–3.21)
Limitations	Quality assessment criteria for prognostic studies as outlined in: Assessing bias in studies of prognostic factors Jill A. Hayden, DC, PhD; Danielle A. van der Windt, PhD; The study sample represents the population of interest on key characteristics, sufficient to limit potential bias to the results (study participation). UNSURE Loss to follow-up (from sample to study population) is not associated with key characteristics, sufficient to limit potential bias (i.e., the study data adequately represent the sample) (study attrition). UNSURE Prognostic factors of interest are measured appropriately in study participants to sufficiently limit potential bias (outcome measurement). NO Outcome measured appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). NO Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest (confounding measurement and account). PARTLY

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	The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results (analysis). YES