### H.2.1.2 Development of geographic atrophy (GA) in people due to AMD: risk outcomes for developing GA

**Ocular risk factors**

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| Cataract surgery | | | | | | | | |
| Chew (2009) Prospective cohort | 5,841 | Very serious[1,2] | N/A | Not serious | Serious[5] | HR (95% CI) | Right eye: 0.80 (0.61, 1.06) Left eye: 0.95 (0.71, 1.26) | VERY LOW |

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| Hyperpigmentation (none as reference category) | | | | | | | | |
| CAPT (2008) Prospecti ve cohort | 1,052 | Serious[1] | N/A | Not serious | Not serious | HR (95% CI) | <250 um: 2.82 (1.30, 6.12)<br>>=250 um: 10.4 (4.51, 24.0) | MODERATE |
| Hyperpigmentation | | | | | | | | |
| Klein (2007) | 3,917 | Serious[1,3] | N/A | Not serious | Not serious | Time-adjusted odds ratios (95% CI) | Increased pigment present vs absent: 15.8 (7.6, 32.8) | MODERATE |
| Retinal pigment epithelium depigmentation | | | | | | | | |
| Klein (2007) Prospecti ve cohort | 3,917 | Serious[1,3] | N/A | Not serious | Not serious | Time-adjusted odds ratios (95% CI) | RPE depigmentation present vs absent: 11.1 (5.0, 24.4) | MODERATE |
| Retinal pigment epithelium depigmentation | | | | | | | | |
| CAPT (2008) Prospecti ve cohort | 1,052 | Serious[1] | N/A | Not serious | Not serious | HR (95% CI) | 2.64 (1.26, 5.53) | MODERATE |
| Pigmentary changes | | | | | | | | |
| Finger (2014) Retrospec tive cohort | 200 | Very serious[1,3,4] | N/A | Not serious | Not serious | HR (95% CI) | Pigmentary Changes: 5.75 (2.09, 15.84) | LOW |
| Pigmentary abnormalities | | | | | | | | |
| Klein (2007) Prospecti | 3,917 | Serious[1,3] | N/A | Not serious | Not serious | Time-adjusted odds ratios (95% CI) | Pigmentary abnormalities present vs absent: | MODERATE |

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| ve cohort | | | | | | | 15.2 (7.3, 31.6) | |
| % of area covered by drusen (<10 as reference category) | | | | | | | | |
| CAPT (2008) Prospecti ve cohort | 1,052 | Serious[1] | N/A | Not serious | Not serious | HR (95% CI) | 10-24%: 2.39 (1.44, 3.97) >=25%: 5.10 (2.57, 10.1) | MODERATE |
| Drusen area | | | | | | | | |
| Klein (2007) Prospecti ve cohort | 3,917 | Serious[1,3] | N/A | Not serious | Not serious | Time-adjusted odds ratios (95% CI) | Drusen area >16877 µm² vs ≤2596 µm²: 24.0 (3.2, 179) | MODERATE |
| Large drusen | | | | | | | | |
| Finger (2014) Retrospec tive cohort | 200 | Very serious[1,3,4] | N/A | Not serious | Not serious | HR (95% CI) | Drusen ≥125µm: 11.73 (1.47, 93.81) | LOW |
| Large drusen | | | | | | | | |
| Klein (2007) Prospecti ve cohort | 3,917 | Serious[1,3] | N/A | Not serious | Not serious | Time-adjusted odds ratios (95% CI) | Drusen > 125µm vs <63µm in diameter: 14.5 (5.9, 35.7) | MODERATE |
| Soft distinct drusen vs hard distinct drusen | | | | | | | | |
| Klein (2007) Prospecti ve cohort | 3,917 | Serious[1,3] | N/A | Not serious | Very serious[6] | Time-adjusted odds ratios (95% CI) | 1.2 (0.3, 5.7) | VERY LOW |
| Soft indistinct vs soft distinct drusen or hard distinct drusen | | | | | | | | |

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| Klein (2007) Prospective cohort | 3,917 | Serious[1,3] | N/A | Not serious | Not serious | Time-adjusted odds ratios (95% CI) | 14.6 (6.8, 31.1) | MODERATE |
| Reticular drusen vs Soft distinct drusen | | | | | | | | |
| Klein (2008) Prospective cohort | 3,917 | Serious[1,3] | N/A | Not serious | Not serious | Time-adjusted odds ratios (95% CI) | 41.78 (9.43, 185.14) | MODERATE |
| Reticular drusen vs Soft indistinct drusen | | | | | | | | |
| Klein (2008) Prospective cohort | 3,917 | Serious[1,3] | N/A | Not serious | Not serious | Time-adjusted odds ratios (95% CI) | 6.23 (1.70, 22.73) | MODERATE |
| Reticular pseudodrusen | | | | | | | | |
| Finger (2014) Retrospective cohort | 200 | Very serious[1,3,4] | N/A | Not serious | Not serious | HR (95% CI) | Reticular pseudodrusen: 4.93 (1.06, 22.93) | LOW |
| Baseline visual acuity (20/25-20/40 as reference category) | | | | | | | | |
| Grunwald (2014) Prospective cohort | 1,024 | Serious[3] | N/A | Not serious | Not serious | HR (95% CI) | 20/50–20/80: 1.66 (1.14, 2.44) 20/100–20/160: 1.70 (1.10, 2.62) 20/200–20/320: 2.65 (1.43, 4.93) | LOW |
| Retinal angiomatous proliferation lesion | | | | | | | | |
| Grunwald | 1,024 | Serious[3] | N/A | Not serious | Not serious | HR (95% CI) | 1.69 (1.16, 2.47) | MODERATE |

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| (2014) Prospective cohort | | | | | | | | |
| Geographic atrophy in fellow eye | | | | | | | | |
| Grunwald (2014) Prospective cohort | 1,024 | Serious[3] | N/A | Not serious | Not serious | HR (95% CI) | 2.07 (1.40, 3.08) | MODERATE |

1. Evidence of bias from study attrition (for example, the paper is not clear about how many people were lost to follow up in the study and/or had missing data, there was no meaningful comparison between those lost to follow up or with missing data in the study and the rest of the included sample)
2. Evidence of bias from outcome measurement (for example, the paper is not clear about how the outcome was measured and what investigations were used, there appears to be no masking or confirmation with multiple readers, outcomes were taken from healthcare database codes where there is likely to be inconsistency in measurement or definition)
3. Evidence of bias from study sample (for example, the paper is not clear about how many people were eligible for the study and were not included, there was no meaningful comparison between those included in the study and the population of interest for important differences)
4. Evidence of bias from confounding factor measurement (for example, the paper is not clear about how the confounding factors were measured, it is not clear which confounders were adjusted for in analysis, not all the important confounders were adjusted for)
5. Downgraded one level for non-significant effect
6. Downgraded two levels for confidence interval crossing 2 lines of a defined minimal important difference

**Demographic and medical risk factors**

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| Hypertension | | | | | | | | |
| CAPT (2008) Prospective cohort | 1,052 | Serious[1] | N/A | Not serious | Not serious | HR (95% CI) | Suspected: 1.01 (0.76, 1.35) Definite: 1.98 (1.16, 3.39) | MODERATE |
| Age (50-59 years as reference category) | | | | | | | | |
| CAPT | 1,052 | Serious[1] | N/A | Not serious | Not serious | HR (95% CI) | 60-69 years: | MODERATE |

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| (2008) Prospective cohort | | | | | | | 6.09 (1.72, 21.5)<br>70-79 years:<br>4.12 (1.18, 14.4)<br>>79:<br>6.39 (1.64, 24.9) | |
| Age | | | | | | | | |
| Klein (2007) Prospective cohort | 3,917 | Serious[1,2] | N/A | Not serious | Not serious | Time-adjusted odds ratios (95% CI) | Age (by increasing categories, 43-54 years, 55-64 years, 65-74 years, 75-86 years): 4.2 (2.9, 6.1) | MODERATE |
| Diabetes mellitus | | | | | | | | |
| Hahn (2013) Retrospective cohort | 6,621 | Very Serious[1,3,4,5] | N/A | Not serious | Serious[6] | HR (95% CI) | 1.03 (0.97 1.09) | VERY LOW |
| Long term use of aspirin | | | | | | | | |
| Klein (2012) Prospective cohort | 4,926 | Not serious | N/A | Not serious | Serious[6] | HR (95% CI) | Regular aspirin use: 1.65 (0.91, 2.99) | MODERATE |
| Smoking | | | | | | | | |
| Klein (2008) Prospective cohort | 2,119 | Serious[1,2] | N/A | Not serious | Very Serious[7] | Time-adjusted odds ratios (95% CI) | Past vs never smokers:<br>0.88 (0.41, 1.88)<br>Current vs never smokers:<br>0.18 (0.02, 1.40) | VERY LOW |

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| History of MI | | | | | | | | |
| Klein (2013) Prospecti ve cohort | 1,700 | Serious[2] | N/A | Not serious | Very Serious[7] | Time-adjusted odds ratios (95% CI) | 0.61 (0.07, 5.34) | VERY LOW |
| History of CVD | | | | | | | | |
| Klein (2013) Prospecti ve cohort | 1,700 | Serious[2] | N/A | Not serious | Very Serious[7] | Time-adjusted odds ratios (95% CI) | 1.31 (0.32, 5.27) | VERY LOW |
| History of angina | | | | | | | | |
| Klein (2013) Prospecti ve cohort | 1,700 | Serious[2] | N/A | Not serious | Very Serious[7] | Time-adjusted odds ratios (95% CI) | 1.53 (0.30, 7.85) | VERY LOW |
| Exercise (sedentary as reference group) | | | | | | | | |
| Knudtson (2006) Prospecti ve cohort | 3,684 | Very Serious[1,2,3] | N/A | Not serious | Very Serious[7] | Time-adjusted odds ratios (95% CI) | Active: 1.1 (0.5, 2.3) | VERY LOW |

1. Evidence of bias from study attrition (for example, the paper is not clear about how many people were lost to follow up in the study and/or had missing data, there was no meaningful comparison between those lost to follow up or with missing data in the study and the rest of the included sample)
2. Evidence of bias from study sample (for example, the paper is not clear about how many people were eligible for the study and were not included, there was no meaningful comparison between those included in the study and the population of interest for important differences)
3. Evidence of bias from prognostic factor measurement (for example, the paper is not clear about how the factor was measured, factors that require definition (e.g. hypertension) were not defined, arbitrary or questionable cut off points were used for continuous values)
4. Evidence of bias from outcome measurement (for example, the paper is not clear about how the outcome was measured and what investigations were used, there appears to be no masking or confirmation with multiple readers, outcomes were taken from healthcare database codes where there is likely to be inconsistency in measurement or definition)
5. Evidence of bias from confounding factor measurement (for example, the paper is not clear about how the confounding factors were measured, it is not

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| clear which confounders were adjusted for in analysis, not all the important confounders were adjusted for)<br>6. Downgraded one level for non-significant effect<br>7. Downgraded two levels for confidence interval crossing 2 lines of a defined minimal important difference | | | | | | | | |

**Diet and nutrition**

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| Daily Alcohol consumption, g (0 as reference category) | | | | | | | | |
| Boekhoorn (2008) Prospective cohort | 4,229 | Serious[1,2] | N/A | Not serious | Serious[4] | HR (95% CI) | ≤10:<br>1.10 (0.32, 3.80)<br>>10 to ≤20<br>1.38 (0.31, 6.16)<br>>20:<br>3.27 (0.88, 12.19) | LOW |
| Total Fat, g (quintile 1 as reference category) | | | | | | | | |
| Reynolds (2013) Prospective cohort | 4,165 | Very serious[1,2,3] | N/A | Not serious | Serious[4] | HR (95% CI) | Quintile 2:<br>1.14 (0.82, 1.59)<br>Quintile 3:<br>0.99 (0.70, 1.39)<br>Quintile 4:<br>1.54 (1.13, 2.11)<br>Quintile 5:<br>1.18 (0.85, 1.64) | VERY LOW |
| Saturated Fat, g (quintile 1 as reference category) | | | | | | | | |
| Reynolds (2013) Prospective cohort | 4,165 | Very serious[1,2,3] | N/A | Not serious | Serious[4] | HR (95% CI) | Quintile 2:<br>1.09 (0.78, 1.51)<br>Quintile 3:<br>1.42 (1.03, 1.95)<br>Quintile 4: | VERY LOW |

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 1.18 (0.85, 1.64)<br>Quintile 5:<br>1.19 (0.87, 1.64) | |
| Monounsaturated Fat g (quintile 1 as reference category) | | | | | | | | |
| Reynolds (2013)<br>Prospecti ve cohort | 4,165 | Very serious[1,2,3] | N/A | Not serious | Not serious | HR (95% CI) | Quintile 2:<br>1.37 (0.98, 1.91)<br>Quintile 3:<br>1.22 (0.86 , 1.71)<br>Quintile 4:<br>1.38 (0.99, 1.94)<br>Quintile 5:<br>1.47 (1.05 , 2.05) | LOW |
| Total Polyunsaturated Fatty Acids g (quintile 1 as reference category) | | | | | | | | |
| Reynolds (2013)<br>Prospecti ve cohort | 4,165 | Very serious[1,2,3] | N/A | Not serious | Serious[4] | HR (95% CI) | Quintile 2:<br>0.95 (0.68, 1.33)<br>Quintile 3:<br>1.10 (0.80, 1.52)<br>Quintile 4:<br>1.34 (0.97,1.85)<br>Quintile 5:<br>1.13 (0.82, 1.55) | VERY LOW |
| Omega-3 fatty acids, Eicosapentaenoic Acid (EPA) - quintile 1 as reference category | | | | | | | | |
| Reynolds (2013)<br>Prospecti ve cohort | 4,165 | Very serious[1,2,3] | N/A | Not serious | Serious[4] | HR (95% CI) | Quintile 2:<br>0.92 (0.65, 1.30)<br>Quintile 3:<br>1.16 (0.86, 1.58)<br>Quintile 4:<br>1.00 (0.71, 1.39) | VERY LOW |

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Quintile 5:<br>0.84 (0.59, 1.18) | |
| Omega-3 fatty acids, Docosahexaenoic Acid (DHA) (g) - quintile 1 as reference category | | | | | | | | |
| Reynolds (2013)<br>Prospective cohort | 4,165 | Very serious[1,2,3] | N/A | Not serious | Serious[4] | HR (95% CI) | Quintile 2:<br>0.99 (0.73, 1.36)<br>Quintile 3:<br>1.14 (0.84, 1.53)<br>Quintile 4:<br>0.93 (0.68, 1.27)<br>Quintile 5:<br>0.72 (0.52, 1.01) | VERY LOW |
| Omega-3 fatty acids, DHA + EPA (g) - quintile 1 as reference category | | | | | | | | |
| Reynolds (2013)<br>Prospective cohort | 4,165 | Very serious[1,2,3] | N/A | Not serious | Serious[4] | HR (95% CI) | Quintile 2:<br>0.98 (0.70, 1.38)<br>Quintile 3:<br>1.20 (0.88, 1.64)<br>Quintile 4:<br>0.91 (0.64, 1.29)<br>Quintile 5:<br>0.79 (0.55, 1.12) | VERY LOW |
| Omega-3 fatty acids, Linolenic Acid (g) - quintile 1 as reference category | | | | | | | | |
| Reynolds (2013) | 4,165 | Very serious[1,2,3] | N/A | Not serious | Serious[4] | HR (95% CI) | Quintile 2:<br>0.90 (0.64, 1.23)<br>Quintile 3:<br>1.02 (0.74, 1.42)<br>Quintile 4:<br>1.06 (0.77, 1.47)<br>Quintile 5: | VERY LOW |

| Studies | Sample size | Risk of bias | Inconsistency | Indirectness | Imprecision | Effect measure | Effect size | Quality |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 1.08(0.80, 1.46) | |
| Omega-6 Fatty Acids, linoleic acid (g) - quintile 1 as reference category | | | | | | | | |
| Reynolds (2013) Prospective cohort | 4,165 | Very serious[1,2,3] | N/A | Not serious | Serious[4] | HR (95% CI) | 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) | VERY LOW |
| Omega-6 Fatty Acids, Arachidonic Acid (g) - quintile 1 as reference category | | | | | | | | |
| Reynolds (2013) Prospective cohort | 4,165 | Very serious[1,2,3] | N/A | Not serious | Serious[4] | HR (95% CI) | 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) | VERY LOW |

1. Evidence of bias from study sample (for example, the paper is not clear about how many people were eligible for the study and were not included, there was no meaningful comparison between those included in the study and the population of interest for important differences)
2. Evidence of bias from study attrition (for example, the paper is not clear about how many people were lost to follow up in the study and/or had missing data, there was no meaningful comparison between those lost to follow up or with missing data in the study and the rest of the included sample)
3. Evidence of bias from prognostic factor measurement (for example, the paper is not clear about how the factor was measured, factors that require definition (e.g. hypertension) were not defined, arbitrary or questionable cut off points were used for continuous values)
4. Downgraded one level for non-significant effect