H.2.1.1 Development of early AMD in people at risk: risk outcomes for developing early AMD

Ocular risk factors

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Large drusen								
Klein (2007) Prospective cohort	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	Drusen > 125µm vs <63µm in diameter: 5.5 (3.5, 8.7)	MODERATE
Soft distinct drusen vs hard distinct drusen								
Klein (2007) Prospective cohort	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	Soft distinct drusen vs hard distinct drusen: 3.0 (2.2, 4.1)	MODERATE
Drusen area								
Klein (2007) Prospective cohort	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	Drusen area >16877 µm² vs ≤2596 µm²: 5.2 (3.7, 7.5)	MODERATE

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)

Demographic and medical risk factors

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Gender								
Klein (2008) Prospecti	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	Female: 2.8 (1.6, 4.9)	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
ve cohort								
Increasing education								
Klein (2008) Prospecti ve cohort	3,917	Serious[1,2]	N/A	Not serious	Serious[5]	Time-adjusted odds ratios (95% CI)	Increasing education 0.6 (0.4, 0.8)	LOW
Obesity (BMI)								
Howard (2014) Prospecti ve cohort	2,641	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	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) 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)	MODERATE
Long term use of aspirin								
Klein (2012) Prospecti ve cohort	4,926	Not serious	N/A	Not serious	Serious[6]	HR (95% CI)	Regular aspirin use: 0.86 (0.71, 1.05)	MODERATE
Age								
Klein	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted	Age (by increasing	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
(2007) Prospective cohort						odds ratios (95% CI)	categories, 43-54 years, 55-64 years, 65-74 years, 75-86 years): 2.3 (2.1, 2.6)	
Age								
Klein (2008) Prospective cohort	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	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)	MODERATE
Smoking								
Klein (2008) Prospective cohort	3,917	Serious[1,2]	N/A	Not serious	Serious[5]	Time-adjusted odds ratios (95% CI)	Past vs never smokers: 1.16 (0.91, 1.48) Current vs never smokers: 1.47 (1.08, 1.99)	LOW
Smoking								
Seddon (2015)* Prospective cohort	2,951	Very Serious[1,2,3,4]	N/A	Not serious	Not serious	HR (95% CI)	Past: 1.1 (1.0, 1.3) Current: 1.8 (1.4, 2.3)	LOW
Smoking								
Klein (2008) Prospective cohort	3,917	Serious[1,2]	N/A	Not serious	Serious[5]	Time-adjusted odds ratios (95% CI)	Current vs never smoker 1.9 (1.03, 3.6) Past vs never smoker 1.4 (0.9, 2.3)	LOW
Smoking								

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Seddon (2013)* Prospective cohort	2,914	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	Past: 1.2 (1.1, 1.4) Current: 1.6 (1.3, 2.1)	MODERATE
Smoking								
Seddon (2013)* Prospective cohort	980	Serious[1,2]	N/A	Not serious	Serious[6]	HR (95% CI)	Past: 1.0 (0.8, 1.4) Current: 2.2 (1.4, 3.3)	LOW
Diabetes history								
Klein (2008) Prospective cohort	3,917	Serious[1,2]	N/A	Not serious	Serious[5]	Time-adjusted odds ratios (95% CI)	0.1 (0.02, 0.8)	LOW
History of MI								
Klein (2013) Prospective cohort	1,700	Serious[1]	N/A	Not serious	Very Serious[7]	Time-adjusted odds ratios (95% CI)	1.13 (0.60, 2.14)	VERY LOW
History of stroke								
Klein (2013) Prospective cohort	1,700	Serious[1]	N/A	Not serious	Very Serious[7]	Time-adjusted odds ratios (95% CI)	1.25 (0.46, 3.38)	VERY LOW
History of CVD								
Klein (2013) Prospective cohort	1,700	Serious[1]	N/A	Not serious	Very Serious[7]	Time-adjusted odds ratios (95% CI)	0.79 (0.46, 1.37)	VERY LOW

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
History of angina								
Klein (2013) Prospective cohort	1,700	Serious[1]	N/A	Not serious	Very Serious[7]	Time-adjusted odds ratios (95% CI)	0.90 (0.48, 1.71)	VERY LOW
Exercise								
Knudtson et al (2006) Prospective cohort	3,684	Very Serious[1,2,3]	N/A	Not serious	Serious[5]	Time-adjusted odds ratios (95% CI)	Sedentary: reference Active: 0.9 (0.7, 1.1)	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. 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. Downgraded one level for confidence interval crossing 1 line of a defined minimal important difference
6. Downgraded one level for non-significant effect
7. Downgraded two levels for confidence interval crossing 2 lines of a defined minimal important difference

*Seddon (2011), Seddon (2013) and Seddon (2015) all report the same participants fros the ARED2 study

Diet and nutrition

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Increased wine drinking								
Klein	3,917	Serious[1,2]	N/A	Not serious	Serious[3]	Time-adjusted	Increased wine	LOW

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
(2008) Prospective cohort						odds ratios (95% CI)	drinking 0.6 (0.3, 1.1)	
Daily Alcohol consumption, g (none as reference category)								
Boekhoorn (2008) Prospective cohort	4,229	Serious[1,2]	N/A	Not serious	Serious[4]	HR (95% CI)	≤10: 1.00 (0.76, 1.30) >10 to ≤20: 0.98 (0.70, 1.36) >20: 1.10 (0.80, 1.51)	LOW
Beta-carotene (quartile 1 as reference category)								
Chiu (2009) Prospective cohort	2,924	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	Q2 (1.5–2.2 mg/day): 1.02 (0.85, 1.22) Q3 (2.2–3.2 mg/day): 0.98 (0.80, 1.18) Q4 (>3.2 mg/day): 0.97 (0.77, 1.21)	MODERATE
Docosahexaenoic acid (quartile 1 as reference category)								
Chiu (2009) Prospective cohort	2,924	Serious[1]	N/A	Not serious	Serious[4]	HR (95% CI)	Q2 (26.0–41.9 mg/day): 1.13 (0.95, 1.34) Q3 (41.9–64.0 mg/day): 0.98 (0.81, 1.18) Q4 (>64.0 mg/day): 1.09 (0.88, 1.35)	LOW
Eicosapentaenoic acid (quartile 1 as reference category)								
Chiu (2009)	2,924	Serious[1]	N/A	Not serious	Serious[4]	HR (95% CI)	Q2 (12.7–24.6 mg/day):	LOW

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Prospecti ve cohort							1.07 (0.90, 1.28) Q3 (24.6–42.3 mg/day): 1.01 (0.84, 1.21) Q4 (>42.3 mg/day): 1.01 (0.83, 1.23)	
Low Glycaemic Index (>81.5 as reference category)								
Chiu (2009)	2,924	Serious[1]	N/A	Not serious	Serious[4]	HR (95% CI)	78.6–81.5: 1.15 (0.96, 1.38) 75.2–78.6: 1.05 (0.87, 1.28) 75.2: 1.03 (0.83, 1.29)	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. Downgraded one level for confidence interval crossing 1 line of a defined minimal important difference
4. Downgraded one level for non-significant effect