H.2.1.4 Development of late AMD in people at risk: risk outcomes for developing any late AMD (GA or CNV)

Ocular risk factors

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Large drusen								
Finger (2014) Retrospective cohort	200	Very serious[1,2,3]	N/A	Not serious	Not serious	HR (95% CI)	Drusen ≥125µm: 2.08 (1.25, 3.49)	LOW
Large drusen in the fellow eye (<250 µm in diameter in the fellow eye as the reference category)								
SST (2009)	370	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	Drusen ≥250 µm in diameter in the fellow	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Prospecti ve cohort							eye: 2.32 (1.49, 3.61)	
Large drusen								
Klein (2007) Prospecti ve cohort	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	Drusen > 125µm vs <63µm in diameter: 29.6 (14.4, 60.7)	MODERATE
Large drusen								
Klein (2011) Prospecti ve cohort	2,846	Very serious[1,2,3]	N/A	Not serious	Not serious	HR (95% CI)	1.79 (1.50, 2.14)	LOW
Largest drusen size in non-advanced eye (<63 µm as reference category)								
Seddon (2011)* Prospecti ve cohort	2,937	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	63-124: 4.1 (1.9, 9.2) 125-249: 7.3 (3.4,15.8) ≥250: 11.7 (5.4, 25.3)	MODERATE
Large drusen in the fellow eye with CNV (<250 µm as reference category)								
SST (2009) Prospecti ve cohort	370	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	Drusen ≥250 µm in diameter: 1.73 (1.12, 2.66)	MODERATE
Size of drusen for those with no advanced AMD in either eye (<63 µm in both eyes as reference category)								
Seddon (2011)* Prospecti ve cohort	2,937	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	L eye, R eye 63–124, <63: 3.5 (1.9, 6.3) 63–124, 63–124: 7.6 (4.2, 13.5)	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
							125–249,<63: 7.8 (4.1, 14.7) 125–249, 63–124: 15.1 (8.8, 25.7) 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)	
Drusen area								
Klein (2011) Prospective cohort	2,846	Very serious[1,2,3]	N/A	Not serious	Not serious	HR (95% CI)	Drusen area >16877 µm² vs ≤2596 µm²: 32.3 (7.8, 133)	LOW
Advanced AMD in one eye: largest drusen size in non-advanced eye, µm (<63 as reference category)								
Seddon (2015)* Prospective cohort	2,951	Very Serious[1,2,4,5]	N/A	Not serious	Not serious	HR (95% CI)	63–124: 3.9 (1.7, 8.6) 125–249: 8.4 (3.9, 18.3) ≥250: 13.8 (6.4, 29.5)	LOW
No advanced AMD: largest drusen size in each eye, µm (<63 µm in both eyes as reference category)								

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Seddon (2015)* Prospective cohort	2,951	Very Serious[1,2,4,5]	N/A	Not serious	Not serious	HR (95% CI)	L eye, R eye 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)	LOW
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: 3.6 (1.5, 8.6)	MODERATE
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[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	17.5 (10.3, 29.8)	MODERATE
Reticular drusen vs Soft distinct drusen								
Klein (2008) Prospective cohort	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	28.29 (9.48, 84.44)	MODERATE
Reticular drusen vs Soft indistinct drusen								
Klein (2008) Prospective cohort	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	6.34 (2.28, 17.63)	MODERATE
Reticular pseudodrusen								
Finger (2014) Retrospective cohort	200	Very serious[1,2,3]	N/A	Not serious	Serious[6]	HR (95% CI)	1.20 (0.76, 1.89)	VERY LOW
Pigmentary changes								
Finger (2014) Retrospective cohort	200	Very serious[1,2,3]	N/A	Not serious	Not serious	HR (95% CI)	2.55 (1.64, 3.96)	LOW
Pigmentary abnormalities								
Klein (2007)	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios	Pigmentary abnormalities present	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Prospecti ve cohort						(95% CI)	vs absent: 10.8 (6.5, 18.0)	
Hyperpigmentation								
Klein (2007) Prospecti ve cohort	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	Increased pigment present vs absent: 9.8 (5.9, 16.3)	MODERATE
Hyperpigmentation in a fellow eye with CNV (no focal hyperpigmentation as reference category)								
SST (2009) Prospecti ve cohort	370	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	Mild/moderate focal hyperpigmentation: 1.43 (0.86, 2.40) Severe focal hyperpigmentation: 2.26 (1.30, 3.94)	MODERATE
Retinal pigment epithelium depigmentation								
Klein (2007) Prospecti ve cohort	3,917	Serious[1,2]	N/A	Not serious	Not serious	Time-adjusted odds ratios (95% CI)	RPE depigmentation present vs absent: 10.5 (5.9, 18.5)	MODERATE
Retinal pigment epithelium depigmentation								
SST (2009) Prospecti ve cohort	370	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	1.79 (1.14, 2.82)	MODERATE
Advanced age related macular degeneration in 1 eye								
Klein (2011) Prospecti ve cohort	2,846	Very serious[1,2,3]	N/A	Not serious	Not serious	HR (95% CI)	1.21 (1.02, 1.45)	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Advanced AMD in 1 eye								
Seddon (2011)* Prospective cohort	2,937	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	1 eye with geographic atrophy: 7.3 (2.9, 18.4) 1 eye with neovascular disease: 5.1 (2.1, 12.2)	MODERATE
Advanced AMD in one eye								
Seddon (2015)* Prospective cohort	2,951	Very Serious[1,2,4,5]	N/A	Not serious	Not serious	HR (95% CI)	Grade 4: 8.3 (3.2, 19.9) Grade 5: 5.8 (2.3, 13.2)	LOW
Geographic atrophy in the fellow eye with CNV								
SST (2009) Prospective cohort	370	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	1.82 (1.08, 3.08)	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)
3. 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)
4. 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)
5. 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)
6. Downgraded one level for non-significant effect

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

Demographic and medical risk factors

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Low dose aspirin								
Christen (2009) Prospective cohort	39,876	Very serious[1,2,3]	N/A	Not serious	Serious[6]	HR (95% CI)	0.90 (0.53, 1.52)	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: 1.21 (0.84, 1.74)	MODERATE
Obesity (BMI)								
Howard (2014) Prospective cohort	2,641	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	Female, non-smoker BMI (per 2.5 kg/m²): 1.31 (1.15, 1.50) Male, non-smoker BMI (per 2.5 kg/m²): 0.86 (0.61, 1.20) Female smoker BMI (per 2.5 kg/m²): 0.99 (0.81, 1.21)	MODERATE
Obesity (BMI)								
Lechanteur (2012) Prospective cohort	108	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	Overweight (25–30): 1.3 (0.8, 2.1) Obese (≥30): 2.2 (1.1, 4.1)	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Obesity (BMI) - <25 as reference category								
Seddon (2003) Prospecti ve cohort	261	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	25-29: 2.32 (1.32, 4.07) ≥30: 2.35 (1.27, 4.34)	MODERATE
Obesity (BMI) - <25 as reference category								
Seddon (2011)* Prospecti ve cohort	2,937	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	25–29: 1.1 (0.9, 1.3) ≥30: 1.3 (1.1, 1.6)	MODERATE
Obesity (BMI) - <25 as reference category								
Seddon (2013)* Prospecti ve cohort	2,914	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	25–29: 1.1 (0.9, 1.3) ≥30: 1.3 (1.1, 1.6)	MODERATE
Obesity (BMI) - <25 as reference category								
Seddon (2015)* Prospecti ve cohort	2,951	Very serious[1,2,3,4]	N/A	Not serious	Not serious	HR (95% CI)	25–29: 1.1 (0.9, 1.3) ≥30: 1.2 (1.0, 1.5)	LOW
Current smoker								
Klein (2011) Prospecti ve cohort	2,846	Very serious[1,2,5]	N/A	Not serious	Not serious	HR (95% CI)	1.78 (1.37, 2.31)	LOW
Smoking								
Seddon (2003) Prospecti	261	Serious[1]	N/A	Not serious	Serious[6]	HR (95% CI)	Past: 1.32 (0.82, 2.12) Current: 1.99 (0.90, 4.43)	LOW

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
ve cohort								
Smoking (pack years) – 0 to 1 as reference category								
Lechanteur (2012) Prospective cohort	108	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	1 to 40: 2.4 (1.3, 4.5) ≥40: 4.4 (1.4, 14.3)	MODERATE
Smoking								
Seddon (2011)* Prospective cohort	2,937	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	Past: 1.1 (1.0, 1.3) Current: 1.8 (1.4, 2.3)	MODERATE
Family History of AMD								
Klein (2011) Prospective cohort	2,846	Very serious[1,2,5]	N/A	Not serious	Not serious	HR (95% CI)	1.40 (1.16, 1.70)	LOW
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): 3.5 (2.8, 4.4)	MODERATE
Age (<65 as reference category)								
Lechanteur (2012) Prospective cohort	108	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	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)	MODERATE
Age (<65 as reference category)								
Seddon	2,937	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	65–74: 1.4 (1.1, 1.7)	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
(2011)* Prospective cohort							≥75: 1.8 (1.5, 2.3)	
Age (<65 as reference category)								
Seddon (2013)* Prospective cohort	2,914	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	65-74: 1.4 (1.1, 1.7) ≥75: 2.0 (1.6, 2.5)	MODERATE
Age (<65 as reference category)								
Seddon (2013)* Prospective cohort	980	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	65-74: 1.5 (1.0, 2.3) ≥75: 2.6 (1.7, 4.1)	MODERATE
Age (≥75 as reference category)								
Seddon (2015)* Prospective cohort	2,951	Very serious[1,2,3,4]	N/A	Not serious	Not serious	HR (95% CI)	65–74: 0.8 (0.6, 0.9) 55–64: 0.6 (0.5, 0.7)	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)	1.04 (0.36, 3.02)	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)	1.33 (0.59, 3.01)	VERY LOW
History of angina								

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Klein (2013) Prospective cohort	1,700	Serious[1]	N/A	Not serious	Very serious[7]	Time-adjusted odds ratios (95% CI)	0.89 (0.32, 2.50)	VERY LOW
Cardiovascular disease								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Serious[6]	HR (95% CI)	1.21 (0.73, 2.02)	LOW
Gender (male as reference category)								
Lechanteur (2012) Prospective cohort	108	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	Female: 2.6 (1.4, 5.0)	MODERATE
Gender (female as reference category)								
Seddon (2011)* Prospective cohort	2,937	Serious[1]	N/A	Not serious	Serious[6]	HR (95% CI)	Male: 1.0 (0.9, 1.2)	LOW
Gender (female as reference category)								
Seddon (2013)* Prospective cohort	2,914	Serious[1,2]	N/A	Not serious	Serious[6]	HR (95% CI)	Male: 1.0 (0.8, 1.1)	LOW
Gender (female as reference category)								
Seddon (2013)* Prospective cohort	980	Serious[1,2]	N/A	Not serious	Serious[6]	HR (95% CI)	Male: 1.0 (0.8, 1.2)	LOW

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Gender (female as reference category)								
Seddon (2015)* Prospective cohort	2,951	Very serious[1,2,3,4]	N/A	Not serious	Serious[6]	HR (95% CI)	Male: 1.1 (0.9, 1.2)	VERY LOW
Education (≤ high school as reference category)								
Lechanteur (2012) Prospective cohort	108	Serious[1,2]	N/A	Not serious	Serious[6]	HR (95% CI)	> high school: 0.6 (0.4, 1.1)	LOW
Education (≤ high school as reference category)								
Seddon (2011)* Prospective cohort	2,937	Serious[1]	N/A	Not serious	Serious[6]	HR (95% CI)	> high school: 0.9 (0.8, 1.0)	LOW
Education (≤ high school as reference category)								
Seddon (2013)* Prospective cohort	2,914	Serious[1,2]	N/A	Not serious	Serious[6]	HR (95% CI)	> high school: 0.9 (0.8, 1.0)	LOW
Education (≤ high school as reference category)								
Seddon (2013)* Prospective cohort	980	Serious[1,2]	N/A	Not serious	Serious[6]	HR (95% CI)	> high school: 0.8 (0.6, 1.0)	LOW
Education (high school as reference category)								
Seddon (2015)* Prospecti	2,951	Very serious[1,2,3,4]	N/A	Not serious	Serious[6]	HR (95% CI)	> high school: 0.9 (0.8, 1.0)	VERY LOW

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
ve cohort								

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 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)
4. Evidence of bias from the 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)
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 clear which confounders were adjusted for in analysis, not all the important confounders were adjusted for)
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
Daily Alcohol consumption, g (0 as reference category)								
Boekhoorn (2008) Prospective cohort	4,229	Serious[1,2]	N/A	Not serious	Serious[3]	HR (95% CI)	≤10: 1.00 (0.53, 1.89) >10 to ≤20: 0.77 (0.33, 1.80) >20: 1.01 (0.46, 2.21)	LOW
Dietary glycaemic index (quintile 1 as reference category)								
Chiu (2007) Prospective cohort	3,977	Serious[1,2]	N/A	Not serious	Not serious	HR (95% CI)	Quintile 2: 1.12 (0.90, 1.40) Quintile 3: 1.14 (0.90, 1.44) Quintile 4:	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
							1.20 (0.94, 1.52) Quintile 5: 1.39 (1.08, 1.79)	
Low dietary glycaemic index (>81.5 as reference category)								
Chiu (2009) Prospecti ve cohort	2,924	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	78.6–81.5: 0.80 (0.67, 0.97) 75.2–78.6: 0.77 (0.63, 0.94) 75.2: 0.76 (0.60, 0.96)	MODERATE
Beta-carotene (quartile 1 as reference category)								
Chiu (2009) Prospecti ve cohort	2,924	Serious[1]	N/A	Not serious	Serious[3]	HR (95% CI)	Q2 (1.5–2.2 mg/day): 0.97 (0.80, 1.19) Q3 (2.2–3.2 mg/day): 1.11 (0.90, 1.37) Q4 (>3.2 mg/day): 1.24 (0.96, 1.59)	LOW
Docosahexaenoic acid (quartile 1 as reference category)								
Chiu (2009) Prospecti ve cohort	2,924	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	Q2 (26.0–41.9 mg/day): 0.97 (0.80, 1.18) Q3 (41.9–64.0 mg/day): 1.04 (0.85, 1.28) Q4 (>64.0 mg/day): 0.73 (0.57, 0.94)	MODERATE
Eicosapentaenoic acid (quartile 1 as reference category)								
Chiu	2,924	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	Q2 (12.7–24.6	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
(2009) Prospective cohort							mg/day): 0.91 (0.75, 1.11) Q3 (24.6–42.3 mg/day): 1.03 (0.85, 1.24) Q4 (>42.3 mg/day): 0.74 (0.59, 0.94)	
Total fat (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	2nd quartile: 1.27 (0.63, 2.53) 3rd quartile: 2.29 (1.08, 4.88) 4th quartile: 2.90 (1.15, 7.32)	MODERATE
Animal fat (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Serious[3]	HR (95% CI)	2nd quartile: 0.81 (0.41, 1.57) 3rd quartile: 1.14 (0.55, 2.37) 4th quartile: 2.29 (0.91, 5.72)	LOW
Vegetable fat (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	2nd quartile: 1.64 (0.86, 3.13) 3rd quartile: 2.27 (1.12, 4.59) 4th quartile: 3.82 (1.58, 9.28)	MODERATE

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
Saturated fat (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Serious[3]	HR (95% CI)	2nd quartile: 0.97 (0.49, 1.93) 3rd quartile: 1.46 (0.66, 3.20) 4th quartile: 2.09 (0.83, 5.28)	LOW
Monounsaturated fat (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Serious[3]	HR (95% CI)	2nd quartile: 1.27 (0.65, 2.45) 3rd quartile: 2.13 (1.03, 4.43) 4th quartile: 2.21 (0.90, 5.47)	LOW
Polyunsaturated fat (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	2nd quartile: 1.57 (0.82, 3.02) 3rd quartile: 1.90 (0.94, 3.84) 4th quartile: 2.28 (1.04, 4.99)	MODERATE
Transunsaturated fat (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	2nd quartile: 1.67 (0.83, 3.36) 2nd quartile: 3.22 (1.63, 6.36) 3rd quartile: 2.39 (1.10, 5.17)	LOW

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
No. of servings of fish a week (<1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Serious[3]	HR (95% CI)	1: 1.30 (0.78, 2.16) ≥2: 0.88 (0.49, 1.60)	LOW
High-fat dairy (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Serious[3]	HR (95% CI)	2nd quartile: 2.08 (1.09, 3.97) 3rd quartile: 1.80 (0.96, 3.38) 4th quartile: 1.91 (0.98, 3.73)	LOW
Meat (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Serious[3]	HR (95% CI)	2nd quartile: 1.75 (0.91, 3.34) 3rd quartile: 1.62 (0.81, 3.24) 4th quartile: 2.09 (0.98, 4.47)	LOW
Processed baked goods (quartile 1 as reference category)								
Seddon (2003) Prospective cohort	261	Serious[1]	N/A	Not serious	Not serious	HR (95% CI)	2nd quartile: 1.21 (0.69, 2.26) 3rd quartile: 2.02 (1.06, 3.85) 4th quartile: 2.42 (1.21, 4.84)	MODERATE
Number of servings of nuts per week (<1 as reference category)								
Seddon	261	Serious[1]	N/A	Not serious	Serious[3]	HR (95% CI)	1: 0.69 (0.40, 1.17)	LOW

Studies	Sample size	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect measure	Effect size	Quality
(2003) Prospective cohort							≥2: 0.60 (0.32, 1.02)	
Taking antioxidants (clinical trial)								
Seddon (2011)* Prospective cohort	2,937	Serious[1]	N/A	Not serious	Serious[3]	HR (95% CI)	0.9 (0.8, 1.0)	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 non-significant effect

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