Age-related vision loss risk assessment tool: Can this improve your business?

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Director of Sightrisk Ltd.
Disclosures

- ALCON (I-CAPS): Research Grants & Consultancy Work
- Novartis (Vitalux): Research Grants & Consultancy Work
- Macuvision Europe (Macushield): Research Grants & Consultancy Work
- Kemin Health (Marigold extracts): Research Grants & Consultancy Work
- Zeiss (Visucam measuring device): Research Grants & Consultancy Work
- Macular Metrics (Densitometer device): Consultancy Work
- Howard Foundation (Meso-Zeaxanthin): Research Grants
- Bausch & Lomb (Ocuvite Preservision; Ocuvite Lutein):  Research Grants & Consultancy Work
- Sightrisk Ltd (Company Director)

Scientific Independence and Editorial Control
Age-related Macular Degeneration

Normal Healthy Macula

AMD Diseased Macula

Normal Vision

AMD Vision
AMD is the leading cause of blindness in the developed world

- Increasing world population
- Increasing longevity
Family History

• **Familial Aggregation Studies**

  • **First-degree relatives** of individuals with any form of AMD (early or late) was over **twice** that in individuals who had no family history of disease (Seddon et al 1997)
  
  • BDES – incidence data
  
  • Rotterdam Eye Study – prevalence data
  
  • Confirmed significant increased risk in association with positive family history
Family History

- **Twin Studies**
  - Monozygotic twins –
    - disease concordance in 100% (Meyers 1994 & 1998)
    - disease concordance in 37% (Hammond 2002)
  - Dizygotic twins –
    - disease concordance in 25% (Meyers 1994 & 1998)
    - disease concordance in 19% (Hammond 2002)

- **Seddon et al. 2005** developed a model for genetic and environment factors and concluded that genetic factors played a significant role in the etiology of AMD accounting for 46% to 71% of the variation in the overall severity of the disease.
Family History

• Gene Studies

  • Complement Factor H (CFH Y402H) gene; AMD risk gene confirmed by three different groups (2005)
    • Odds ratio ranging of 2.45 to 3.33 for all stages of AMD
    • Odds ratio ranging of 3.47 to 7.4 for late AMD

  • ARMS2/LOC387715 gene; believed to relate to mitochondrial function

  • Multiplicative effect: Homozygosity for this risk gene, in combination with homozygosity for the CFH Y402H allele, confers an odds ratio of 57.6 (95% CI: 37.2–89.0) for the development of AMD, when compared to the non-risk genotype
Cigarette Smoking

Average odds ratio: 2.4

76% of studies reporting a statistically significant negative impact of smoking
Cigarette Smoking

AMD Aetiopathogenic mechanism

• Promote vascular changes in the eye
  • May represent an antecedent common to both Atherosclerosis and AMD

• Reduce circulating levels of antioxidants

• Increased pro-oxidant load

• Reduced macular pigment
### Average odds ratio: 1.49

50% of studies reporting a statistically significant negative association with obesity
Obesity

• Antecedent common to both cardiovascular disease and AMD
• Link with inflammation
• Obese people may have a decreased dietary intake of important nutrients
• Impair antioxidant defence mechanisms within the retina (e.g. macular pigment)
Average odds ratio: 1.41

50% of studies reporting a statistically significant negative association with light exposure
Light exposure

- The retina is subjected to high levels of cumulative irradiation with visible light over a lifetime
- Difficult to accurately measure cumulative and lifetime exposure to visible light
  - There is a growing consensus that cumulative lifetime exposure to visible light increases the risk of AMD
  - EUREYE study: Blue light and low antioxidants significantly increase risk of AMD (Fletcher et al. 2008)
Other putative risk factors for AMD

• **Cardiovascular disease** – common link with AMD e.g. Risk factors – however, data remains inconsistent

• **Diabetes Mellitus** – recent suggestion of significant relationship with AMD

• **Hypertension** – increases AMD (majority of studies)

• **Plasma lipids** – evidence unimpressive, with few reports confirming an association between hyperlipidaemia and AMD:
  • serum cholesterol was associated with a 2.2-fold increased risk of neovascular AMD in the EDCCS

• **Female sex hormones** – data inconclusive
Other putative risk factors for AMD

- **Physical inactivity** – people with active lifestyles are at less risk of AMD but most likely due to other factors (e.g. smoking, diet)
- **Refractive error** – increased scleral thickness – vascular hypothesis – increased risk of AMD data inconsistent
- **Iris colour** – non-blue eyes have increased melanin and may protect against AMD – strong suggestion of link between eye colour and increased risk of AMD
- **Alcohol consumption**
  - wine: phenolic compounds – beneficial for AMD
  - beer: nitrosamines – toxic – increase risk of AMD
  - relationship with lifestyle is important
Nutrition and AMD

Studies investigating the relationship between nutrition and AMD

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>No. of cases</th>
<th>Design</th>
<th>Age group</th>
<th>Nutritional data</th>
<th>ARM/Nutrient relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHANES I</td>
<td>1988</td>
<td>3,082</td>
<td>Cohort</td>
<td>45 to 74</td>
<td>FFQ* (vitamin A and C)</td>
<td>Inverse</td>
</tr>
<tr>
<td>EDCCS</td>
<td>1994</td>
<td>1,994</td>
<td>Case-control</td>
<td>55 to 80</td>
<td>FFQ (66-item)</td>
<td>Inverse</td>
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<tr>
<td>BDES</td>
<td>1996</td>
<td>1,968</td>
<td>Cohort</td>
<td>45 to 86</td>
<td>FFQ (100-item)</td>
<td>None</td>
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<tr>
<td>BDES</td>
<td>1998</td>
<td>1,586</td>
<td>Population-based cohort</td>
<td>43 to 86</td>
<td>FFQ (100-item)</td>
<td>Inverse</td>
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<tr>
<td>BMES</td>
<td>1999</td>
<td>3,654</td>
<td>Cross-sectional</td>
<td>49 +</td>
<td>FFQ (145-item)</td>
<td>None</td>
</tr>
<tr>
<td>NHANES II</td>
<td></td>
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<tr>
<td>BMES</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>NHS &amp; HPFS</td>
<td>2004</td>
<td>118,428</td>
<td>Prospective follow-up</td>
<td>50 +</td>
<td>FFQ (vitamins &amp; carotenoids)</td>
<td>Inverse</td>
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<td>AREDS</td>
<td>2007</td>
<td>4,513</td>
<td>Case-control</td>
<td>55 to 80</td>
<td>FFQ (carotenoids, L &amp; Z)</td>
<td>Inverse</td>
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<tr>
<td>BMES</td>
<td>2007</td>
<td>2,454</td>
<td>Population-based cohort</td>
<td>49 +</td>
<td>FFQ (145-item, L &amp; Z)</td>
<td>Inverse</td>
</tr>
</tbody>
</table>

Over 80% of studies reporting a positive and statistically significant association between nutrition and AMD.
Serum nutrition and AMD

Studies investigating the relationship between serum nutrition and AMD

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>No. of cases/No of controls</th>
<th>Design</th>
<th>Age group</th>
<th>Nutritional data</th>
<th>ARM/Serum antioxidant relationship</th>
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</thead>
<tbody>
<tr>
<td>Blumenkranz et al.</td>
<td>1986</td>
<td>26/23</td>
<td>Case-control</td>
<td>-</td>
<td>Vit. A, C and E</td>
<td>none</td>
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<tr>
<td>Tsang et al.</td>
<td>1992</td>
<td>80/86</td>
<td>Case-control</td>
<td>-</td>
<td>Vit. E &amp; selenium</td>
<td>none</td>
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<td>EDCCS</td>
<td>1992</td>
<td>421/615</td>
<td>Case-control</td>
<td>-</td>
<td>Carotenoids</td>
<td>inverse</td>
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<tr>
<td>EDCCS</td>
<td>1993</td>
<td>421/615</td>
<td>Case-control</td>
<td>55 to 80</td>
<td>Vit. C, E carotenoids &amp; zinc</td>
<td>inverse</td>
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<tr>
<td>BLSA</td>
<td>1994</td>
<td>870</td>
<td>Cohort</td>
<td>40+</td>
<td>Vits., retinol, and b-carotene</td>
<td>inverse</td>
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<tr>
<td>BDES</td>
<td></td>
<td></td>
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<tr>
<td>BMES</td>
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<tr>
<td>Belda et al.</td>
<td>1999</td>
<td>25/15</td>
<td>Case-control</td>
<td>60+</td>
<td>Vit. E &amp; zinc</td>
<td>inverse</td>
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<tr>
<td>POLA</td>
<td>1999</td>
<td>2584</td>
<td>Cross-sectional</td>
<td>-</td>
<td>Vit. E</td>
<td>inverse</td>
</tr>
<tr>
<td>NHANES III</td>
<td>2001</td>
<td>8222</td>
<td>Cross-sectional</td>
<td>40+</td>
<td>L &amp; Z (combined)</td>
<td>inverse</td>
</tr>
<tr>
<td>Gale et al.</td>
<td>2003</td>
<td>380</td>
<td>Cross-sectional</td>
<td>66 to 75</td>
<td>L &amp; Z (separate)</td>
<td>inverse (Z only)</td>
</tr>
</tbody>
</table>

Over 80% of studies reporting a positive and statistically significant association between serum nutrition and AMD
Studies investigating the macular carotenoids for AMD

### Interventional Studies

<table>
<thead>
<tr>
<th>Principal Author</th>
<th>Study</th>
<th>Year</th>
<th>n</th>
<th>Study Design</th>
<th>Age</th>
<th>Carotenoids</th>
<th>Finding</th>
</tr>
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<tbody>
<tr>
<td>Richer et al</td>
<td>-</td>
<td>1999</td>
<td>14</td>
<td>Case Series</td>
<td>61-79</td>
<td>L (14mg)</td>
<td>Improved VP</td>
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<tr>
<td>Olmedilla et al</td>
<td>-</td>
<td>2001</td>
<td>5</td>
<td>Case Series</td>
<td>69-75</td>
<td>L (15mg)</td>
<td>Improved VP</td>
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<tr>
<td>Richer et al</td>
<td>LAST</td>
<td>2004</td>
<td>90</td>
<td>RCT</td>
<td>68-82</td>
<td>L (10mg)</td>
<td>Beneficial‡</td>
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<tr>
<td>Bartlett et al</td>
<td>-</td>
<td>2007</td>
<td>25</td>
<td>RCT</td>
<td>55-82</td>
<td>L (6mg)</td>
<td>No benefit</td>
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<tr>
<td>Chakravarthy et al</td>
<td>CARMA</td>
<td>2007</td>
<td>433</td>
<td>RCT</td>
<td>50+</td>
<td>L (12mg) &amp; Z (0.6mg)</td>
<td>Beneficial‡</td>
</tr>
</tbody>
</table>

### Observational Dietary Studies

<table>
<thead>
<tr>
<th>Principal Author</th>
<th>Study</th>
<th>Year</th>
<th>n</th>
<th>Study Design</th>
<th>Age</th>
<th>Carotenoids</th>
<th>Nutrient/AMD relationship</th>
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</thead>
<tbody>
<tr>
<td>Seddon et al</td>
<td>EDCCS</td>
<td>1994</td>
<td>356/520*</td>
<td>Case Control</td>
<td>55-80</td>
<td>L&amp;Z</td>
<td>Inverse</td>
</tr>
<tr>
<td>VandenLangenberg et al</td>
<td>BDES</td>
<td>1996</td>
<td>1968</td>
<td>Cohort</td>
<td>45-86</td>
<td>L&amp;Z</td>
<td>None</td>
</tr>
<tr>
<td>Mares-Peelman et al</td>
<td>III</td>
<td>2001</td>
<td>8222</td>
<td>Cross-sectional</td>
<td>40+</td>
<td>L&amp;Z</td>
<td>Inverse</td>
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<tr>
<td>Flood et al</td>
<td>BMES</td>
<td>2002</td>
<td>2335</td>
<td>Cohort</td>
<td>49+</td>
<td>L&amp;Z</td>
<td>None</td>
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<tr>
<td>Snellen et al</td>
<td>-</td>
<td>2002</td>
<td>72/66*</td>
<td>Case Control</td>
<td>60+</td>
<td>L</td>
<td>Inverse</td>
</tr>
<tr>
<td>LaRowe et al</td>
<td>CAREDS</td>
<td>2006</td>
<td>1787</td>
<td>Cross-sectional</td>
<td>50-79</td>
<td>L&amp;Z</td>
<td>None</td>
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<tr>
<td>San Giovanni et al</td>
<td>AREDS</td>
<td>2007</td>
<td>4519</td>
<td>Case Control</td>
<td>60-80</td>
<td>L&amp;Z</td>
<td>Inverse</td>
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<tr>
<td>Tan et al</td>
<td>BMES</td>
<td>2007</td>
<td>2454</td>
<td>Cohort</td>
<td>49+</td>
<td>L&amp;Z</td>
<td>Inverse</td>
</tr>
</tbody>
</table>

### Observational Serum Studies

<table>
<thead>
<tr>
<th>Principal Author</th>
<th>Study</th>
<th>Year</th>
<th>n</th>
<th>Study Design</th>
<th>Age</th>
<th>Carotenoids</th>
<th>Nutrient/AMD relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>EDCCS</td>
<td>1993</td>
<td>421/615*</td>
<td>Case Control</td>
<td>-</td>
<td>L&amp;Z</td>
<td>Inverse</td>
</tr>
<tr>
<td>Mares-Peelman et al</td>
<td>BDES</td>
<td>1995</td>
<td>167/167*</td>
<td>Case Control</td>
<td>43-86</td>
<td>L&amp;Z</td>
<td>None</td>
</tr>
<tr>
<td>Mares-Peelman et al</td>
<td>III</td>
<td>2001</td>
<td>8222</td>
<td>Cross-sectional</td>
<td>40+</td>
<td>L&amp;Z</td>
<td>Inverse</td>
</tr>
<tr>
<td>Simonelli et al</td>
<td>-</td>
<td>2002</td>
<td>48/46*</td>
<td>Case Control</td>
<td>mean=67</td>
<td>L&amp;Z</td>
<td>None</td>
</tr>
<tr>
<td>Gale et al</td>
<td>-</td>
<td>2003</td>
<td>380</td>
<td>Cross-sectional</td>
<td>66-75</td>
<td>L&amp;Z, L; Z</td>
<td>Inverse (Z only)</td>
</tr>
<tr>
<td>Cardinault et al</td>
<td>-</td>
<td>2005</td>
<td>34/21*</td>
<td>Case Control</td>
<td>72-74</td>
<td>L; Z</td>
<td>None</td>
</tr>
<tr>
<td>Delcourt et al</td>
<td>POLA</td>
<td>2006</td>
<td>899</td>
<td>Cohort</td>
<td>60+</td>
<td>L&amp;Z</td>
<td>Inverse (esp. Z)</td>
</tr>
<tr>
<td>Fletcher et al</td>
<td>EES</td>
<td>2008</td>
<td>2283/2117*</td>
<td>Cross-sectional</td>
<td>65+</td>
<td>L; Z</td>
<td>Inverse (esp. Z)</td>
</tr>
</tbody>
</table>
Risk factors for AMD

Established
• Age
• Smoking
• Family history

Putative
• Diet
• Light
• Obesity
• Cardiovascular disease
• Low macular pigment levels
• White ethnicity

Adapted from Cai et al., Progress into Retinal and Eye Research, 2000 Mar; 19(2):205-21
Conclusions: Overall, the prevalence of any AMD in the 2005-2008 National Health and Nutrition Examination Survey was 6.5%, which is lower than the 9.4% prevalence reported in the 1988-1994 Third National Health and Nutrition Examination Survey. While this finding might be explained in part by possible methodological differences, these estimates are consistent with a decreasing incidence of AMD and suggest important public health care implications.
Conclusions: High dietary intake of nutrients with antioxidant properties reduces the risk of early AMD in those at high genetic risk. Therefore, clinicians should provide dietary advice to young susceptible individuals to postpone or prevent the vision-disabling consequences of AMD.
Conclusions: Modifying lifestyles might reduce risk for early AMD as much as 3-fold, lowering the risk for advanced AMD in a person's lifetime and the social and economic costs of AMD to society.
Pathogenesis of AMD

• Oxidative stress
  • free radicals

• Cumulative blue light damage
  • free radicals

Oxidative stress/blue light damage
Carotenoids

- These are plant pigments found in nature that we consume through fruit and vegetables.
Macular pigment is uniquely located at the macula, the central part of the retina responsible for optimal spatial vision.
Online AMD research study for optometrists: Current practice in the Republic of Ireland and the United Kingdom
Methods

• The Association of Optometrists in Ireland and the College of Optometrists in the UK invited their members to participate in this online AMD survey. 750 emails were circulated in Ireland and 8,049 were circulated in the UK. Reminder emails were sent after 6 weeks.

• The survey was open for a total of 3 months. In total, 724 respondents (8.2%) completed and submitted the survey online.

• The questions in the survey were designed to obtain information regarding AMD assessment techniques and nutritional supplements used to manage AMD.
What assessments do you routinely perform to check for the presence of AMD and/or risk of developing AMD?

- Amsler grid (35%)
- Fundus photography
- MP measurement
- Ophthalmoscopy
- Volke Risk assessment
- OCT
Recommendation of eye supplements

- **91%** of practices stated that they recommend eye supplements to patients with AMD
- **73%** of practices stated that they recommend eye supplements to patients at risk of AMD
- The most commonly recommended supplement was ICaps (53%), followed by Macushield (49%)
- The most cited reason by practices for recommending their chosen supplement was “**strong scientific evidence**”
- **22%** of practices reported some form of **improvement** in at least one of their AMD patients following supplementation
- The reported **improvement** is highest amongst those practices recommending Macushield
AMD Prevention Strategy

- AMD screening service:
  - Macular pigment measurement
  - Fundus photography
  - Genetics testing
  - Visual performance
  - Contrast sensitivity
  - Risk assessment software
Sightrisk can assess your risk of developing age-related blindness. By taking appropriate and informed action, in a timely manner, together we can help to reduce the risk of vision loss.

Login

Welcome To Sightrisk

Sightrisk provides a solution to an international problem: age-related vision loss. Because of increasing life expectancy, age-related blindness is reaching epidemic levels. However, many of these eye conditions can be avoided by making positive lifestyle changes. We provide online risk assessment tools to identify people who are at risk of developing blindness, and provide personalised advice on how to reduce this risk before the disease has a chance to develop.

Two of the eye conditions we specialise in are age-related macular degeneration, more commonly known as AMD, and cataract. These
Science- and evidence-based

- Over 300 peer-reviewed scientific manuscripts
- Built online using over 400 lines of web code
- All known and putative risk factors for AMD
- Results graph: current and optimised risks
- Tailored modifiable risks
Online calculator page

Sightrisk AMD Calculator

Complete the following information to calculate your patient’s predicted risk of developing AMD. Importantly, the more information provided, the stronger the confidence of the predicted risk.

Before performing the calculation, please review the supporting information and definitions relating to each question by clicking on the corresponding symbol: ?

Personal Information

Name: Sarah

Current Age: 26
Age at which to calculate the risk of AMD: 70

Non-ocular and Lifestyle Risks

Genetic Status: Information Unavailable
- Negative
- CFH
- ARMS2
- Both

Family history of visually consequential AMD: No family history of AMD
- Parent / brother / sister with AMD
- Information unavailable

Cigarette smoking: Current smoker - 10 or fewer

Diet (fruit and vegetables): Diet rich in fruit and vegetables
- Diet medium in fruit and vegetables
- Diet low in fruit and vegetables
Predicted AMD Risk

Sarah's current predicted risk of developing AMD which affects vision at the age of 70 is 16%.

Sarah, your personalised modifiable risk factors for AMD are outlined below in order of predicted importance. Please discuss with your eyecare professional the following modifiable risk factors when considering your risk of developing AMD.

1. Take eye-related nutritional supplements which contain the macular carotenoids to promote macular health.
2. Increase your intake of Omega-3: eat coldwater oily fish such as salmon, nuts and seeds such as walnuts and flaxseeds, or take an Omega-3 supplement.
3. Increase your macular pigment level to promote and protect macular health (see your eyecare professional for more advice).
4. Eat more brightly coloured fruits and vegetables, including leafy greens such as spinach and kale, peppers, sweetcorn, oranges and grapes.
5. Eat more fish, especially oily fish, and shellfish.
6. If your genetic status is unknown, your risk may be higher than predicted.

For Eyecare Professionals

Discussion: The AMD Calculator is a practical tool developed by experts in the field and is intended as a supplementary tool to personal risk assessment. Your personal individual risk of developing AMD may be influenced by other factors not considered by the calculator tool. This model should be reviewed in conjunction with your specific risk factors. It is important to consult with your eyecare professional to assess your personal risk of developing AMD and to determine your specific risk factors.
Predicted Risk of Developing AMD at the age of 70 is 24%
Who benefits from Sightrisk?

- **Patients**
  - Reduced risk of AMD
  - Increased awareness of AMD
  - Regular monitoring for AMD risk

- **Practice**
  - Increase sales of additional products (e.g. supplements, sunglasses, photochromic lenses)
  - Increased footfall into the practice
  - Encourages patient loyalty

- **Staff**
  - Improved scientific expertise
  - Improved patient rapport
Financial Benefits

• Increase sales
  • Nutritional supplements
  • Sunglasses
  • Protective lenses
  • Additional AMD services, e.g. fundus photography, macular pigment measurement

• Return visits

• Patient loyalty

Our cost benefit analysis has shown that using Sightrisk just once a week generates up to €6,000 per annum
Visit our AMD Prevention Clinic and reduce your risk of developing AMD

The age-related macular degeneration (AMD) Prevention Clinic assesses an individual’s risk of developing AMD, so that a customised prevention plan to reduce that individual’s risk of developing this condition can be put in place.

Who should attend?

- Adults, especially those with a family history of AMD. Individuals at increased risk of developing AMD include:
  - Individuals with a family history of AMD
  - Individuals who smoke cigarettes
  - Individuals with diets lacking in fruits and vegetables
  - Individuals exposed to large amounts of sunlight on a daily basis
  - Individuals with light colored eyes
  - Individuals who are overweight
  - Individuals with high blood pressure
  - Individuals with high cholesterol

What does it involve?

A typical clinic assessment lasts approximately two hours. The following investigations are used to gather important AMD risk factor information about an individual so that a customized and personalized prevention plan is generated.

- **AMD gene test**: This non-invasive gene test provides important information on whether the individual’s genetic background predisposes to AMD.
- **Fundus photography**: A photograph of the retina (back of the eye) is obtained, allowing the eye specialist to assess the retina for any signs of AMD.
- **Vision testing**: A detailed set of specialised vision tests are conducted to measure visual performance.
- **Microperimetry**: Provides a sensitivity map of retinal function.
- **Optical coherence tomography**: This technology provides important information on the layer structure of the retina.
- **Macular pigment**:
  - The yellow pigment at the retina, known as macular pigment, is measured using a specialised device. This measurement provides important information on the nutritional and antioxidant status of the retina.
- **Sightrisk AMD software technology**:
  - The Sightrisk AMD Calculator is an analytical tool used to assess an individual’s composite risk of developing AMD in the future, by taking into account all of the above information with respect to risk for this condition, and analysing the individual’s risk factors in an evidence-based and appropriately weighted fashion.

Where is the clinic and how can I make an appointment?

**Location:**
Institute of Vision Research, Suite 14, Whitfield Clinic, Cork Road, Co. Waterford, Ireland.

**Phone:** 00 353 (0)51 302153
**Email:** info@ivr.ie
**Website:** www.ivr.ie
Thank you for listening!

Any questions?

Please submit your questions into the webinar chat box (you may need to maximise the webinar window)

Don’t forget to complete the CET /CPD lecture questions at this link:

www.ocuco.co.uk/age-related-vision-loss-risk-assessment-tool-survey.html

Presented by Dr. John Nolan,
Waterford Institute of Technology