Update on Modifiable Risk Factors for Age-related Macular Degeneration

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C-15092 1 CET point for optometrists and dispensing opticians

Background

Age-related macular degeneration (AMD) is the commonest cause of age-related blindness in developed countries, and it is estimated that there are approximately 80 000 people affected by this condition in Ireland, with over 12 million sufferers across Europe. Although the pathogenesis of AMD remains unclear, there is a growing consensus that free radical damage induced by cumulative short-wavelength light (blue) and oxidative stress plays a role in its development (Beatty et al. 2000).

The three undisputed risk factors for AMD are: (1) increasing age; (2) positive family history of disease; and (3) cigarette smoking. Tobacco use is, therefore, the only proven environmental/lifestyle risk factor for this disease (Chakravarthy et al. 2007; Klein et al. 1998; Tan et al. 2007). However, there is a growing body of evidence that other variables are associated with increased risk for AMD and these include white race, dietary deficiency of antioxidants relevant to retinal health, undesirable body mass index (BMI), hypertension (high blood pressure), hypercholesterolaemia and chronic and cumulative exposure to ambient short-wavelength visible light (SanGiovanni et al. 2007; Tomany et al. 2004).

It would appear, therefore, that construction workers in Ireland are at increased risk of developing blindness (ie AMD) in later life, as they are exposed to many of the above-mentioned variables in a way that is not true for their office-based counterparts. Furthermore, and given that we are living in an era of unprecedented and ever-increasing life expectancy, risk for AMD needs to be assessed at a time in the individual's life when preventive measures are likely to reduce such risk. For example, smoking cessation in a 35-year-old male will reduce his risk of developing AMD in later life, but this would not be true if he was to discontinue tobacco use at, say, age 65 years (Cai et al. 2000).

We have conducted a study to evaluate risk for AMD amongst construction workers in Ireland, and to furnish those workers with advice to reduce their risk of developing this condition in a way that is evidence-based and tailored to the individuals' risk profiles.

Methods

A total of 853 subjects were recruited into this study. The study was approved by the local Research Ethics Committee and informed consent was obtained from each subject.

Study data were collected in conjunction with the nurse-led Construction Workers Health Trust (CWHT) health screening service.

Risk factors for AMD

Specifically, information on lifestyle variables, with emphasis on risk factors for AMD, was obtained from each subject by questionnaire, and included: sex, nationality, level of physical activity, diet, intake of nutritional supplements, smoking habits, family history of AMD, childhood and current sun exposure, use of protective eye wear, skin colour, iris colour, hypermetropia, history of cataract surgery, BMI, blood sugar, hypertension, cholesterol, lipoprotein, triglyceride, spirometry and macular pigment (MP).

Nationality

Nationality was split as follows, in order of frequency: Irish, Polish, English, Spanish, Swedish, American, Lithuanian, Portuguese, Scottish, Argentinian, German, Libyan, Moldovan, New Zealand, Northern Irish, Romanian, Slovak, and Ukrainian.

Dietary assessment

An indicator of dietary intake and bioavailability of lutein (L) and zeaxanthin (Z) and other antioxidants was constructed according to the frequency of consumption of the following food items: coloured fruits and vegetables, fish and overall fat intake, with examples given. The frequency of consumption was scored as portion intake per day. Dietary fat intake (eg fried foods, snack foods, cheese, foods cooked in butter) was assessed due to its role in carotenoid absorption from the gut (Roodenburg et al. 2000; Unlu et al. 2005), whereas fish intake was assessed due to its high concentration of n-3 docosahexaenoic acid, which has been shown to influence MP concentration (Snodderly et al. 2005). In this way, an aggregate score for all food items was assigned to each person and used in analysis. The highest possible aggregate score for this analysis was 15.5.

Measurement of macular pigment optical density

MP is located at the macula and is made up of three carotenoids, known as lutein (L), zeaxanthin (Z) and meso-zeaxanthin (MZ). L and Z are entirely of dietary origin, whereas MZ is principally formed in the retina following conversion from L. MP is a short-wavelength (blue) light filter and a powerful antioxidant, and is therefore believed to protect against AMD via these properties. MP's absorption spectrum is such that it filters the damaging short wavelengths of the visible spectrum before they are incident upon the retina, and MP is therefore believed to be uniquely protective for AMD. MP was measured in the right eye only, by heterochromatic flicker photometry using the Macuscope.

Sightrisk

This specialised software, provided by Sightrisk Ltd, was used to generate a predicted percentage risk of development of visually consequential AMD at a later stage in life. The software calculates an individual's predicted percentage risk of developing AMD at any given age between 55 and 100 years by using the individual's risk factors entered to generate an evidence-based cumulative risk factor index as a percentage. The software also provides advice to modify positively current risk factors and reduce the individual's risk of developing AMD. The risk factor weightings are based on the results of over 300 peer-reviewed manuscripts. Each subject was provided with advice to modify positively their lifestyle with the aim of reducing their AMD risk following the assessment.

We have determined the threshold of visual difficulty at 6/12 as 'visually consequential' AMD; the reasoning behind this is that 6/12 is a borderline level for safe driving, and below 6/12 one has trouble with everyday tasks. Although there are various other signs of vision loss, such as loss of contrast and general blurring, visual acuity is generally the most accepted method of measurement (albeit not the most appropriate measure of vision).

The Sightrisk results are displayed in a graph and as a predicted percentage risk ranging from 5% to 95% at the age of 70 (Figure 1).

The predicted risk for this hypothetical participant of developing visually consequential AMD at the age of 70 is 21%. The health care professional would discuss the information and modifiable risks (below) with the patient and provide appropriate advice.
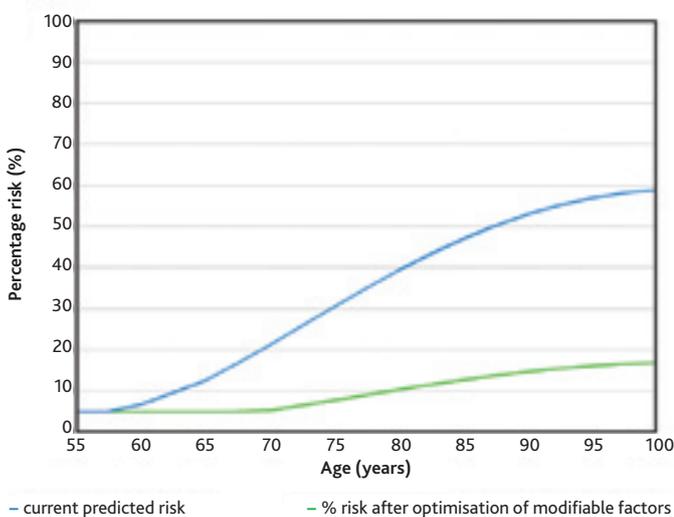
Figure 1. Cumulative predictive risk factor index for visually consequential age-related macular degeneration.

Mr Murphy's predicted risk of developing visually consequential AMD at the age of 70 is 21%.

Mr Murphy, your modifiable risk factors include:

- Cigarette smoking – cigarette smoking is associated with increased risk of AMD
- Diet – a diet rich in fruit and vegetables is associated with reduced risk of AMD

- MP – low MP levels are associated with increased risk of AMD
- Cumulative exposure to visible light – high lifetime exposure to light is associated with increased risk of AMD: the use of protective eye wear is advised
- BMI – a BMI of <25 is associated with reduced risk of AMD
- Cholesterol – high cholesterol levels are associated with increased risk of AMD

These modifiable risk factors are weighted in order of importance based on the results of over 300 scientific research studies.

Iris colour

Iris colour was categorised into light or dark as follows:

- Light blue, blue, grey, light green, green = light
- Hazel, light brown, brown, black = dark

Light exposure

Light exposure was quantified as the amount of time subjects stated that they spent outside during daylight hours. This was categorised as follows:

- Low = largely indoors
- Medium = 50:50 indoors:outdoors
- High = largely outdoors

Physical activity

All subjects were asked how often they exercised or played sports for at least 20 minutes (examples included brisk walking, cycling, swimming, jogging or aerobics) and the answers were categorised as number of times per week ranging from 5 to 0. Subjects were also asked how much hard physical work was required at their job, and the answers were categorised as: a great deal, a moderate amount, a little, or none. In this way an aggregate score for all physical activity was assigned to each person and used in analysis. The highest possible aggregate score for this analysis was 7.

Known family history of AMD

All subjects were asked whether any of their parents or siblings have or had AMD at any stage throughout their lives.

Statistical analysis

The statistical analysis software package SPSS (version 18) was used for statistical and graphical analysis. All variables investigated exhibited a typical normal distribution. Means ± standard deviation (SD) are presented in text and tables. Independent sample t-tests were used to compare mean differences and Pearson correlation coefficients were used to compare the relationship between bivariables, as appropriate. We used 5% level of significance throughout analysis.
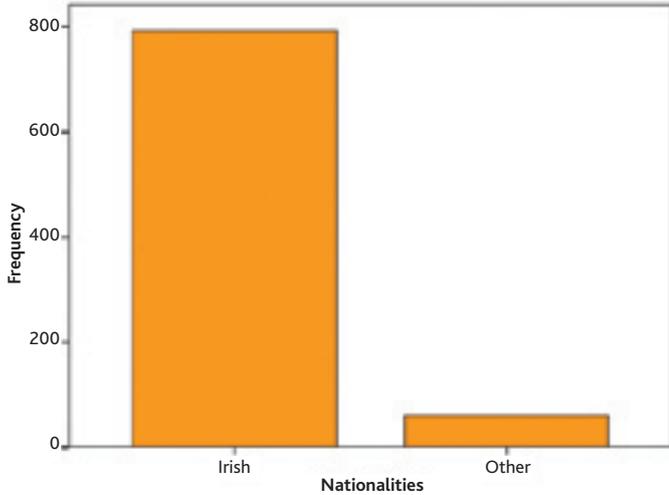
Results

Univariate exploratory analysis

Age

The mean ± SD age of the subjects recruited into the study was 34 ± 13 years.

Nationality

In this study 792 (92.8%) subjects were of Irish nationality, 56 (6.6%) were of other European nationalities and 5 (0.5%) were of North American, South American, North African and Australasian nationalities (Figure 2).
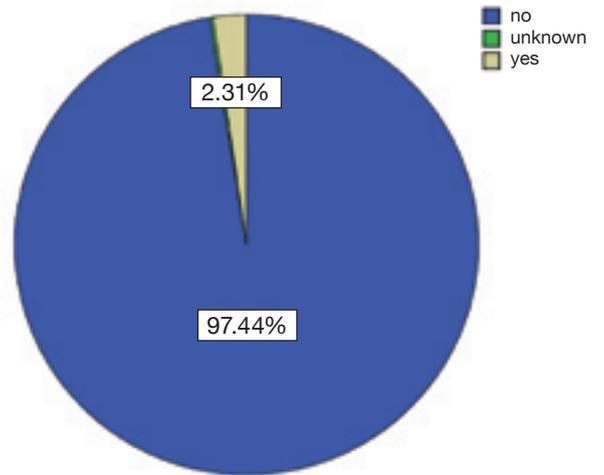

Figure 2. Distribution of nationalities.

Sex

In all, 826 (96.8%) of the subjects recruited into the study were male and 27 (3.2%) were female.

Known family history of AMD

A total of 800 (93.8%) subjects stated that they had no known family history of AMD, 2 (0.2%) stated that they did not know their family history of AMD and 19 (2.2%) stated that they did have a family history of AMD (Figure 3).

Body mass index

The mean ± SD BMI of the study group was 26.3 ± 3.91.

Diet

The mean ± SD aggregate score (representative of dietary intake of carotenoids) was 4.93 ± 2.35. The highest possible aggregate score for this analysis was 15.5.
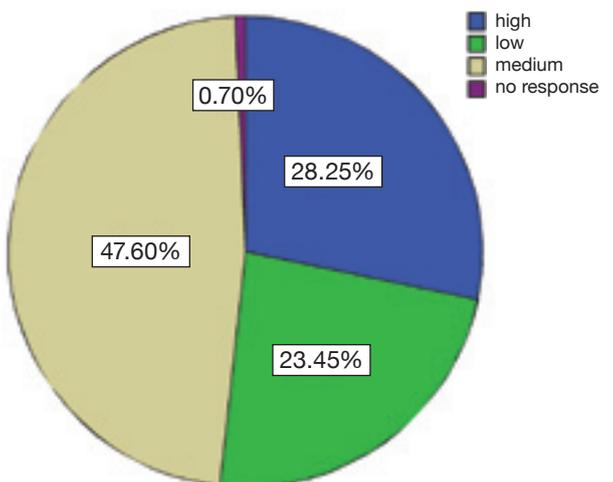
Macular pigment optical density (MPOD)

The mean ± SD MPOD of the study group was 0.46 ± 0.19.

Sightrisk

The mean ± SD Sightrisk-predicted percentage risk at the age of 70 was calculated as 20.1 ± 10.2. The accepted and published prevalence of AMD in the normal global population (ie which includes all ethnicities) at the age of 70 is only 10% (Klein et al. 1997). Of note, therefore, the average construction worker in Ireland is at twice the risk of developing AMD when compared to the general population (*P* < 0.05).

Iris colour

A total of 667 (78.2%) subjects stated that they had light iris colour, and 163 (19.1%) stated that they had dark iris colour.

Use of sunglasses

The use of sunglasses when in sunlight amongst the study group was as follows: 17.6% never wear sunglasses, 18.3% rarely wear sunglasses, 33.3% sometimes wear sunglasses, 14.8% often wear sunglasses and 14.5% always wear sunglasses (Figure 4).

Figure 3. Known family history of age-related macular degeneration AMD).

Figure 4. Use of sunglasses when in sunlight.

Figure 5. Exposure of daylight.

Light exposure

In this study, 241 (28.3%) subjects stated that they had a high exposure to daylight, 406 (47.6%) stated that they had a medium exposure to daylight and 200 (23.4%) stated that they had a low exposure to daylight (Figure 5).

Hypertension

The mean ± SD hypertension of the study group, shown as systolic blood pressure over diastolic (mmHg), was 126.97 ± 13.14 over 74.76 ± 11.20.

Cholesterol

The mean ± SD cholesterol of the study group was 4.13 ± 0.82 mmol/l.

Physical activity

The mean ± SD aggregate score (representative of exercise and physical work) was 4.08 ± 1.88. The highest possible aggregate score for this analysis was 7.

Bivariate analysis

Predicted AMD percentage risk and macular pigment

There was an inverse and statistically significant relationship between predicted percentage risk of AMD development at the age of 70 and MP optical density amongst the construction workers ($r = -0.309$, $P = 0.000$) (Figure 6).

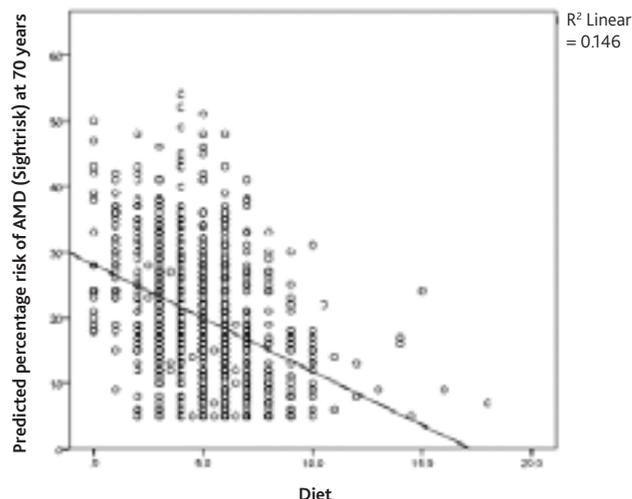### Predicted AMD percentage risk and diet

There was an inverse and statistically significant relationship between predicted percentage risk of AMD development at the age of 70 and dietary intake of nutrients of benefit to eye health amongst the construction workers ($r = -0.382$, $P = 0.000$) (Figure 7).
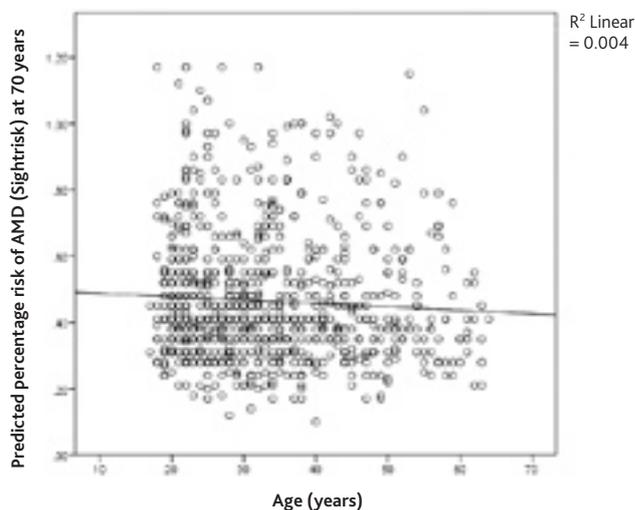
Macular pigment optical density and age

There was an inverse and statistically significant relationship between MP optical density and age amongst the construction workers ($r = -0.071$, $P = 0.041$) (Figure 8).
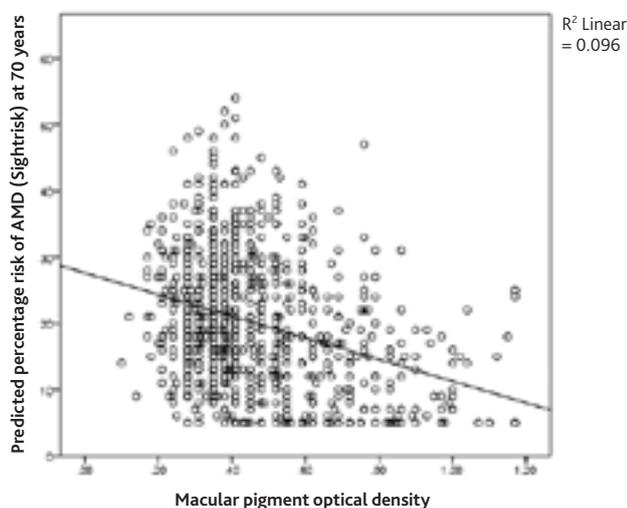
Diet and age

There was a statistically significant relationship between dietary intake of nutrients of benefit to eye health and age amongst the construction workers ($r = 0.145$, $P = 0.000$) (Figure 9).
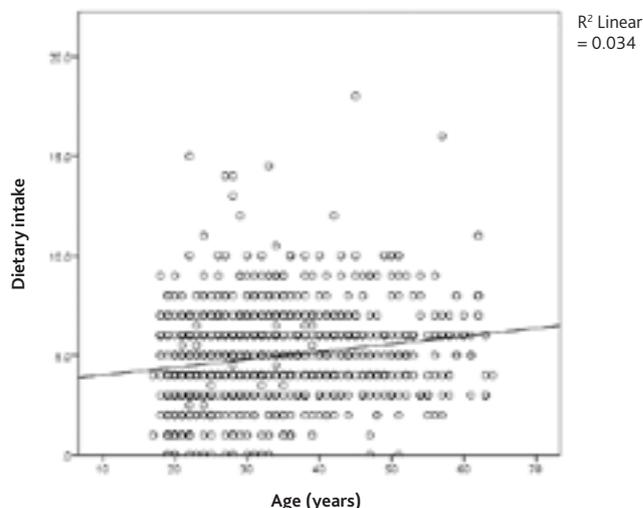

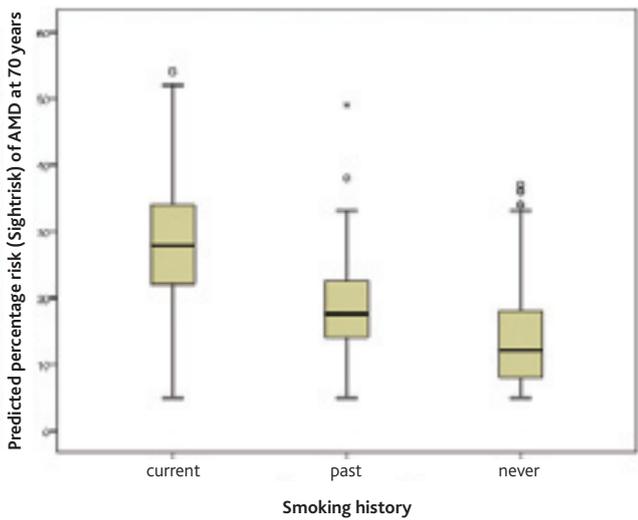**Figure 7.** Predicted age-related macular degeneration (AMD) percentage risk and diet.

Figure 8. Macular pigment optical density and age. AMD, age-related macular degeneration.

Figure 6. Predicted age-related macular degeneration (AMD) percentage risk and macular pigment.

Figure 9. Diet and age.

Figure 10. Predicted age-related macular degeneration (AMD) percentage risk and smoking history.

Predicted AMD percentage risk and smoking history

Current cigarette smokers were at significantly increased predicted risk of developing AMD at the age of 70 years when compared to both past and non-smokers ($P = 0.000$) (Figure 10).

Multivariate analysis

Predicted percentage risk (Sightrisk) of AMD at 70 years

Taking the predicted percentage risk (Sightrisk) of AMD at 70 years as the dependent variable and all other possible contributing AMD risk factors as the predictor variables, including age, sex, known family history, smoking history, diet, BMI, MP, use of sunglasses, exposure to daylight, hypertension, skin colour, nationality, iris colour, cholesterol and physical activity, the following regression model was constructed (Table 1). In brief, we see that the independent predictors of AMD risk in the current study sample include: known family history, smoking history, diet, BMI, MP, iris colour, cholesterol and exposure to daylight.

Macular pigment optical density

Taking MP optical density as the dependent variable and all other possible contributing AMD risk factors as the predictor variables, including age, sex, known family history, smoking history, diet, BMI, predicted percentage risk (Sightrisk) of AMD development at the age of 70, use of sunglasses, exposure to daylight, hypertension, skin colour, nationality, iris colour, cholesterol and physical activity, the following regression model was constructed (Table 2). In brief, we see that the independent predictors of MP optical density in the current study sample include: known family history, smoking history, diet, BMI, predicted percentage risk (Sightrisk) of AMD development at the age of 70, iris colour, cholesterol and exposure to daylight. Of note, these findings are consistent with the widely acknowledged publication by the Macular Pigment Research Group published in *Experimental Eye Research* (Nolan et al. 2007).

Table 1. Dependent variable: predicted percentage risk (Sightrisk) of age-related macular degeneration at 70 years

Model	Coefficients*				
	Unstandardized coefficients		Standardized coefficients		
	B	Standard error	Beta	t	Significance
(Constant)	22.388	1.648		13.586	0.000
Family history	6.032	0.650	0.178	9.283	0.000
Tobacco	−6.711	0.226	−0.583	−29.735	0.000
Diet	−1.512	0.084	−0.350	−18.046	0.000
Body mass index	0.400	0.052	0.152	7.709	0.000
Macular pigment	−14.123	1.025	−0.266	−13.783	0.000
Eye colour	−3.741	0.495	−0.145	−7.555	0.000
Cholesterol	1.406	0.246	0.113	5.715	0.000
Daylight	2.541	0.274	0.180	9.292	0.000

*Dependent variable: Sightrisk.

Table 2. Dependent variable: macular pigment optical density

Model	Coefficients*				
	Unstandardized coefficients		Standardized coefficients		
	B	Standard error	Beta	t	Significance
(Constant)	0.759	0.047		16.175	0.000
Family history	0.076	0.021	0.122	3.635	0.000
Tobacco	−0.079	0.010	−0.364	−8.163	0.000
Diet	−0.024	0.003	−0.296	−8.196	0.000
Body mass index	0.005	0.002	0.108	3.241	0.001
Daylight	0.039	0.009	0.146	4.404	0.000
Sightrisk	−0.014	0.001	−0.735	−14.279	0.000

*Dependent variable: macular pigment.

Conclusion

In conclusion, this large cross-sectional study designed to investigate the risk of AMD amongst the construction workers in Ireland has identified that the average construction worker is at approximately double the risk of predicted AMD development when compared to the normal population. It is clear from the information presented above that there is a need to inform and advise the construction industry on ways of reducing the risk of developing this debilitating eye disease. Of importance, smoking cessation and dietary modification to include leafy greens, coloured fruits and vegetables, and in some cases dietary supplementation containing the macular carotenoids should be advised to reduce risk of AMD. In addition, efforts should be made to reduce cumulative light exposure amongst the construction workers (given that the majority of their work is performed outdoors in the absence of appropriate eye wear protection). It is important to note that, given that AMD is the result of cumulative and chronic insult from light and oxygen metabolism, protection and risk reduction against this disease need to be achieved in a similar manner. In other words, it is important that construction workers in Ireland make positive dietary and lifestyle changes now if they are to reduce their risk of developing AMD in the future.

● Summary

Age-related macular degeneration (AMD) is the commonest cause of age-related blindness in developed countries, and it is now estimated that there are over 12 million AMD sufferers across Europe, a figure that is expected to increase because of the ageing population. Indeed, the number of people with AMD is expected to double in the next 10 years (24 million AMD sufferers by 2020). The current study was designed to evaluate risk for AMD amongst construction workers in Ireland. We hypothesised that construction workers are, uniquely, at increased risk of developing AMD in later life, as they are exposed to many of the known risk factors for AMD in a way that is not true for their office-based counterparts.

In brief, we have identified that the average construction worker is at approximately double the risk of predicted AMD development when compared to the normal population. Of importance, smoking cessation and dietary modification, to include leafy greens, coloured fruits and vegetables, and in some cases dietary supplementation containing the macular carotenoids should be advised to reduce the risk of AMD in construction workers, or individuals with similar environmental and lifestyle traits (eg cigarette smokers, individuals with diet lacking in fruits and vegetables and individuals exposed to high amounts of sunlight).

Acknowledgement

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Multiple choice questions

This paper is reference C-15092. One point is available for optometrists and dispensing opticians. Please use the inserted answer sheet. Copies can be obtained from Optometry in Practice Administration, PO Box 6, Skelmersdale, Lancashire WN8 9FW. There is only one correct answer for each question.

1. Which of the following would not be considered a risk factor for AMD?

(a) Afro-Caribbean race
(b) Increasing body mass index
(c) Hypertension
(d) Chronic exposure to short-wavelength light

2. Regarding macular pigment (MP), which of the following statements is incorrect?

(a) It is made up of three carotenoids
(b) Meso-zeaxanthin is formed in the retina following conversion from zeaxanthin
(c) MP is a short-wavelength light filter
(d) MP density can be measured using a macuscope

3. What visual acuity threshold was regarded as visually consequential for the purpose of the study?

(a) 6/9
(b) 6/12
(c) 6/18
(d) 6/24

4. What percentage of construction workers in the study often wear sunglasses in sunlight ?

(a) 17.6%
(b) 18.3%
(c) 14.8%
(d) 14.5%

5. What was the mean systolic blood pressure of the construction workers in the study?

(a) 117mmHg
(b) 122mmHg
(c) 127mmHg
(d) 132mmHg

6. Which of the following was not shown to be an independent predictor of AMD risk in this study?

(a) Known family history
(b) Iris colour
(c) Exposure to daylight
(d) Race

● CPD Exercise

After reading this article can you identify areas in which your knowledge of the risk of developing AMD has been enhanced?

How do you feel you can use this knowledge to offer better patient advice?

Are there any areas you still feel you need to study and how might you do this?

Which areas outlined in this article would you benefit from reading in more depth, and why?

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