Exploring attitudes towards dietary modification and nutritional supplementation in people with and without age-related macular degeneration

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Age-related macular degeneration (AMD) is the leading cause for visual impairment and blindness registration in the developed world. Due to the large amounts of conflicting AMD research on the role of nutrition and antioxidant intake, it is difficult for patients and practitioners to determine which measures can be taken to slow down the disease progression.

The aim of this research was to determine the beliefs and knowledge that patients with AMD have about nutrition, to identify whether their condition is preventing them from eating a healthy diet, and to discover what their diet consists of.

For the initial study, 158 participants with AMD (mean age 79 ± 7.8 years) and 50 participants without AMD (mean age 67 ± 8 years) were recruited from the Macular Society helpline, or from optometric practice. Participants had a 25 minute telephone interview where a 36-question survey was completed. The survey elicited demographic information, and questions covered the knowledge that participants had on nutrition and their current diet.

The results from this survey uncovered three major findings: 1) 100% of AMD participants felt that they do not have enough information and support from eye-care practitioners regarding nutrition, 2) AMD patients are confused over, and display a lack of knowledge of, which foods are beneficial for eye health and when and what nutritional supplements to take, evidenced by 65% of participants not taking the correct dosage 3) AMD patients are not eating enough nutrients that would be beneficial for their condition - consuming an average of 1.4mg of lutein and zeaxanthin rather than the recommended 10mg.

A clinical decision-making aid was created as an intervention based upon these findings. The aim of the aid was to help eye-care practitioners give the correct nutritional advice to their patients. Founded on the AREDS 2 inclusion and exclusion criteria, practitioners are able to identify which patients could benefit from a nutritional supplement, and which patients could benefit from dietary modification. An evaluation of the aid with 72 qualified eye-care practitioners exhibited a statistically significant increase in confidence after using the aid for two weeks. An evaluation using 51 student optometrists showed a statistically significant increase in confidence and a statistically significant increase in appropriate management of patients after using the aid.

This project has elicited findings that are significant for AMD patient education. It is hoped that through these studies, patients will receive consistent advice about the risk factors for AMD, the link between AMD and nutrition, and the importance of maintaining a healthy, well-balanced diet.

Keywords: age-related macular degeneration, diet, flowchart, nutrition, survey.

For Richard, Alex and Amelia

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Chapter One

Background and literature review

1.1 Introduction to age-related macular degeneration

Loss of vision can be one of the most feared complications of aging [1-4]. For many older people, good vision represents life, autonomy and being active whereas poor vision is associated with depression, fear and loss of activity [3].

Age-related macular degeneration (AMD) is a multifactorial degenerative condition affecting the central area of the retina. It is the leading cause of visual impairment and blindness registration in the developed world [5]. A rapidly aging population has raised the priority of reducing the risk for age related eye diseases that impair sight and quality of life. As there are currently 9.7 million people aged 65 and older in the UK and by 2020 one in five UK citizens will be aged 65 or older (approximately 12 million people) [6], it is imperative that more is learnt about AMD and more is done to help those with the condition.

Aetiology

Central vision, high resolution and fine detail are possible due a critical area of the retina known as the macula. The macula is approximately 5mm in diameter and is central in the retina. The retina consists of two layers, the inner neurosensory retina, and the outer retinal pigment epithelium (RPE) cell layer. The RPE is separated from the outer vascular layer known as the choroid, by Bruch's membrane, an atypical basement membrane. The choroid consists of an internal network of capillaries (choriocapillaris) adjacent to Bruch's membrane, and an external large vessel layer. The retina derives its blood supply from the choroid, as well as an intra-retinal capillary network. Bipolar and ganglion cells help transmit signals to photoreceptor cells, and at the macula they are displaced laterally - this displacement ensures minimal interference with signalling. The fovea, forming the macular centre, is a depression in the inner retinal surface (approximately 1.5mm in diameter) that is thinner and concave in cross-section and contains the highest concentrations of cone photoreceptors [7] (please see **Figure 1.1**).

Age-related macular degeneration is a disease of the outer retina: the damage or loss of photoreceptors, a breakdown of the retinal pigment epithelium (RPE), Bruch's membrane and the choriocapillaris. Much of the damage and/or loss of this area occur in individuals over the

age of 50, hence providing the condition with its name. However, the disease is multifactorial in which multiple genetic and environmental factors are involved.

Figure 1.1. Cross-sectional pathological changes occurring in the macula in (a) Normal macula, (b) Dry AMD and (c) Wet AMD. Copied from [8]

The exact reason for the damage in the outer retina of the macula is still a matter for debate and on-going research. There are also a number of modifiable and non-modifiable risk factors that have been associated with AMD, increasing age and smoking being the two principal influences.

1.2 Progression and Classifications of AMD

The International Classification and Grading System for Age-related Maculopathy (ARM) was introduced in 1995 to standardise classification [9], and has been tested for accuracy [10]. ARM refers to:

- Large soft drusen that can be distinct or indistinct
- Pigmentary abnormalities of the retinal pigment epithelium (RPE) and the retina: either hyperpigmentation in the outer choroid and/or retina, or hypopigmentation of the RPE.

Figure 1.2 ARM, showing soft indistinct drusen across the entire retina. Image from IRI – Illinois Retina Institute.

Age-related macular degeneration (AMD) is the classification used in later stages of the condition. It includes all the clinical signs found in ARM, plus a progression into one of the following forms:

- ‘Dry’ – also known as non-exudative AMD. Manifestations: drusen and sharp, demarcated round/ oval areas of hypopigmentation in the RPE that are at least 175 µm in diameter. Geographic atrophy is advanced dry AMD – focal RPE atrophy leading to loss of the RPE and photoreceptors.
- ‘Wet’ – also known as neovascular/ disciform/ exudative AMD. Manifestations: neovascular membranes (either sub-retinal or sub-RPE), pigment epithelium detachments, sub-retinal haemorrhages, hard exudates and fibrous scarring of the macular.

In 2013, Ferris *et al*. [11] proposed a five stage classification of AMD which achieved consensus among many macular specialists: Stage (1) no apparent ageing changes

(2) normal ageing changes, known as ‘drupelets’ (small drusen ≤ 63 µm)

(3) early AMD– medium-sized drusen 125 ≤µm

(4) intermediate AMD – large drusen and pigmentary (hyper or hypo) anomalies

(5) late AMD – geographic atrophy and/or neovascularisation.

The largest recent clinical trial of supplements for AMD – the Age Related Eye Disease Study (AREDS) [12]– classified AMD using the following system:

Category 1: *No AMD.* No drusen, or a few small drusen (≤ 63 µm in diameter)

Category 2: *Early stage AMD.* Any or all of the following*:* multiple small drusen or a few intermediate drusen (63 – 124 µm in diameter) in one or both eyes, or RPE abnormalities.

Category 3: *Intermediate AMD.* Any or all of the following : extensive intermediate drusen and at least one large drusen (≥ 125 µm in diameter) in one or both eyes, or geographic atrophy not involving the centre of the fovea.

Category 4: *Advanced AMD.* Geographic atrophy (GA) involving the fovea or abnormal and fragile blood vessels under the retina (neovascular form).

The AREDS studies are discussed in length in the sections ‘Clinical Intervention of other Nutrients’ and ‘Lutein and zeaxanthin: a review of evidence’.

Figure 1.3 . Wet AMD, with large sub-retinal haemorrhages over the entire macula area. Image from CNIB (Seeing Through Vision Loss).

1.3 Diagnosis and treatment

Formal diagnosis in the UK occurs via an ophthalmologist after a referral from either an optometrist or the patient's GP. Often, after the initial diagnosis, the patient will receive some written material regarding the disease during their visit to an ophthalmology department. The decision then rests with the ophthalmologist as to whether the patient requires any treatment such as anti-vascular endothelial growth factor therapy (e.g., Lucentis®) or surgery/laser work for 'wet' AMD conditions, low vision services or placement upon a sight impairment register. If the AMD is early or 'dry' type, the patient will have very little contact with any vision professionals for some years – if at all – unless the AMD changes to a 'wet' type. Patients are advised to have a yearly eye examination with an optometrist who will monitor the condition, but is often unable to provide physical or psychological help without referral [13].

1.4 Prevalence

UK prevalence:

The UK has an ageing population - the proportion of the population aged 65 and over has increased over the past 30 years, and this change is projected to continue. This is partly due to

the increase in life expectancy and also due to the relatively high number of births in the years following World War II and during the 1960s, and the impact of these groups moving into the higher age groups [14]. In 2014, 18% of the population was aged 65 or over, in 2024 this is projected to rise to 20%. [14-16]. Currently there are two million people in the UK with sight problems [5].

Owen *et al.*'s estimated that 2.4% of the total population had late stage AMD in 2012, which is equivalent to 513000 cases [16]. They estimate this will increase to 679000 cases by 2020 due to the aging of the population. The prevalence was found to be 4.8% in those aged over 65 years and 12.2% in those aged over 80 years. GA prevalence rates were 1.3%, 2.6% and 6.7%; neovascular AMD 1.2%, 2.5% and 6.3%, respectively. The estimated number of prevalent cases of late AMD were 60% higher in women versus men. The annual incidence of late AMD, GA and neovascular AMD per 1000 women was 4.1, 2.4 and 2.3; in men 2.6, 1.7 and 1.4, respectively. Approximately 71 000 new cases of late AMD were estimated per year.

US prevalence:

One in 28 US adults older than 40 are visually impaired [17]. Adults older than 80 years comprise 8% of US population but account for 70% of cases of severe visual impairment [17]. In 1990, The Beaver Dam Eye Study estimated that there were 640000 people in the US who had signs of late stage AMD, and 95.5% of the over 43 years-of-age population had one or more drusen present in the macular area [18, 19]. It was thought that this number would at least double in 20 years. It is estimated that currently there are 55 million people at risk of having AMD in the US [20]. However, 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[18]. While this finding might be explained in part by differences in study methods, Klein *et al.* controversially hypothesise that these estimates are consistent with a decreasing incidence of AMD [18].

1.5 Hypotheses for the origin of AMD

The current hypotheses can be categorised below:

1) Bruch's membrane changes

Bruch's membrane is a pentalaminar structure composed of several layers of elastic and collagen fibres which separates the RPE from the choriocapillaries - the main blood supply to the outer retina. Nutrients must cross this membrane to enter the RPE and photoreceptors, which is crucial as photoreceptors do not have their own blood supply [21, 22].

Conductivity of Bruch's membrane declines with age, and the lipid content of the membrane increases [23-25]. This, in turn, changes the diffusion characteristics of the membrane which may contribute to the onset of AMD [26].

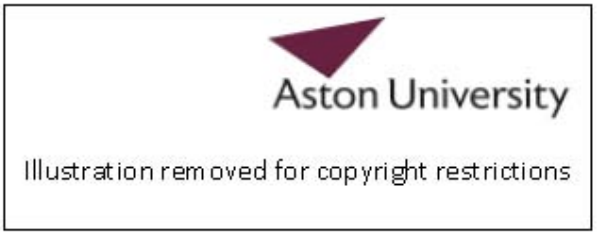


Figure 1.4 Layers of the retina. Bruch's membrane lies between the RPE and the choriocapillaries.[27]

2) Vascular Insufficiency

Changes to the choroidal circulation may affect the normal diffusion of substances and gases across the RPE to Bruch's membrane. Removal of waste products slows down, leading to a build-up of waste materials and a disturbance to the supply of gases and metabolites to the neural retina [25]. The RPE can then deteriorate through ischaemia ('zone hypoxia') or as a direct consequence of the waste material, and the blood flow will decrease. Smith *et al.* [28] hypothesise that since a decreased blood flow is evident in early AMD, the vascular insufficiency theory is supported in the aetiology of AMD.

3) Genetics

Numerous studies have shown there is a genetic predisposition for AMD, as the incidence appears to run in families, and especially in first-degree relatives [28, 29]. The Y402H allele in the complement factor H gene (chromosome 1g31) has been researched as it helps to regulate the body's inflammatory response by protecting against uncontrolled complement activation. The allele's polymorphism appears to exert a strong influence on the risk of developing AMD [30]. There are also many other gene or genes on other chromosomes that have also been research for their ability to modify AMD risk [31]. However, susceptibility is determined by multiple factors that include environmental influences such as UV exposure as well as inherited influences.

Clinicopathogenesis of AMD

The deposition of metabolic debris between the basement membrane of the RPE and Bruch's membrane is often the first clinical feature of an altered retinal metabolic state. This will consist of the outer segments of photoreceptors that have not been metabolised and are in a lipid state (lipofuscin) [32]. This lipid accumulation can be seen as drusen – they also contain proteins such as ubiquitin, inflammatory mediators and advanced glycation end products [33].

4) Oxidative stress hypothesis

Photoreceptors are exposed to an extensive amount of oxidative stress; an imbalance between the systemic production of reactive oxygen species (ROS - chemically reactive molecules containing oxygen), and a biological system's ability to swiftly detoxify the reactive intermediates or to restore the resulting destruction [34]. The retina has antioxidant processes to delay or prevent oxidation (the removal of electrons), but also generates activated forms of oxygen known as free radicals (any atom or molecule that has one or more unpaired electron[35]). Free radicals try to become stable by removing electrons from other molecules,

thereby damaging them and causing a cytotoxic oxidative chain. Other diseases such as Parkinson's disease, cervical cancer and diabetes have been linked with oxidative damage [36].

Researchers have used measurements of thiol metabolites and lipid peroxidation products in plasma to quantify the amount of oxidative stress an individual might have. These are known as oxidative biomarkers, and they consist of cysteine (a thiolated amino acid), glutathione (a cys-derived antioxidant), cystine, isoprostant and isofuran (lipid peroxidation products) [37]. Studies by Brantley *et al.* have shown that mean plasma levels of these biomarkers appear to be higher in AMD patients than in case-control studies [38].

The eye is particularly susceptible to oxidative damage due to:

1. The high percentage of polyunsaturated fatty acids such as docosahexanoic acid (DHA) that are within the outer membrane of photoreceptors. These have a large amount of electrons due to their double bonding, and therefore can be readily oxidised. This will lead to lipid peroxidation causing loss of function and structural integrity within the membrane. [35]
2. The exposure to light (particularly blue) is a strong oxidising agent, causing free radical production [39] This was found by the extensive work carried out by Ham *et al* on Rhesus monkeys [40], Wiegand *et al.* on albino rats [41] and more recent studies which have shown light damage causes cellular apoptosis, and oxidative stress proteins to be released [42].
3. The eye's oxygen consumption and blood flow is high (higher than the brain in a gram-for-gram basis), thereby making it very active metabolically. [43]
4. It contains chromophores – molecules that absorb light in order to cause a chemical reaction – such as rhodopsin, melanin, lipofuscin and the mitochondrial respiratory enzymes.
5. Retinal pigment epithelial phagocytosis is, in itself, a free radical producing process.

A recent study by Yildirim *et al.* showed that reductions in the antioxidant defence system, increased oxidative stress causing oxidative damage to lipids and proteins, and decreases to antioxidant capacity may lead to irreversible damage in the form of AMD [44].

Figure 1.5. Mechanism of dry and wet AMD formation. Reproduced from 'Nature Reviews Drug Discovery'[45].

1.6 Nutrients and AMD

Antioxidant therapy is an attempt to reduce the number of circulating ROS due to oxidative stress. The antioxidants in the next few paragraphs have been researched for their effect on the progression and development of ARM and/or AMD. A clinical breakthrough in positive antioxidant intervention (a 25% risk reduction) was the aforementioned Age-Related Eye Disease Study (AREDS) in 2001 [12] – this is covered in the 'Clinical Intervention of other Nutrients' section 1.9 – the most current research is AREDS 2, the results of which were released in May 2013 (see 'Lutein and zeaxanthin: a review of evidence' section 1.7).

Recommended Daily Allowances

Recommended Daily/Dietary Allowances (RDA), are recommendations for the *minimum* amount of a nutrient that is needed for most individuals to stay healthy. They were developed by the Food and Nutrition Board of the National Academy of Sciences/National Research Council in the US during World War I, and were updated every five to 10 years. They are different for children, young adults, older adults and males and females [46].

In 1997, RDAs became one part of a wider set of dietary guidelines called the Dietary Reference Intake (DRI) which includes the following nutrient measures as well: Adequate Intakes, known as AI; Estimated Average Intakes, known as EAR; and Tolerable Upper Intake Levels, known as UL.

DRI is becoming the more accepted form for nutrient recommendations in the US. In the UK, many agencies still use RDA or GDA – 'Guideline Daily Amount'.

Nutrients that are considered beneficial for AMD

Vitamin C

This is a water soluble antioxidant that can protect against free radical-mediated oxidative tissue damage. Low levels have been associated with an increased risk of AMD, but high levels have not shown to be protective [47]. The UK's NHS website states that adults need 40mg per day, whereas the National Institute for Health, USA recommends at least 75mg in adults, increasing to 110mg in smokers. See **Appendix 1** for examples of vitamin C rich foods.

Vitamin E

These are a group of eight fat soluble compounds that have many biological functions – the most important being a distinctive antioxidant ability to stop the production of ROS when fat undergoes oxidation. Tocopherol is one of the compounds in the vitamin E group: the four common forms of tocopherol include: α, β, ϒ, and δ. In the human retina, the alpha form is the most predominant in high concentrations [48]. A relationship has been found between high plasma vitamin E levels and a reduced risk of AMD. **Appendix 2** shows the US RDA for US citizens. The UK's NHS website advises that males require 4mg per day, and females require 3mg per day. Please also see **Appendix 3** for examples of vitamin E rich foods.

Zinc

This metallic element is very concentrated in human tissue, especially in the retina and RPE. It is important as it acts as a cofactor for retinal dehydronase and catalase – both of which are antioxidant enzymes. A low concentration of zinc can compromise macrophages and through increased apoptosis, T and B lymphocytes also become reduced. Zinc deficiency can result in an increased vitamin A uptake [49], causing toxicity, and lipid peroxidation and damage to lipid membranes. In the human body, zinc stimulates the protein metallothionein in the intestinal wall, causing it to bind to dietary copper and preventing copper absorption. For this reason, zinc is often supplemented alongside copper. **Appendix 4** shows the US RDA for zinc. The UK RDA of zinc is 5.5 to 9.5 mg for men and 4 to 7 mg for women.

Omega-3 Fatty Acids

Docosahexaenoic acid (DHA) (C22:6 omega-3), the major dietary and structural omega-3 long-chain polyunsaturated fatty acid (LCPUFA) of the retina, may modulate metabolic processes and stop the effects of environmental exposures that activate molecules implicated in the pathogenesis of retinal diseases. These processes and exposures include chronic light exposure, oxidative stress, ischaemia, inflammation, cellular signalling mechanisms, and aging. Eicosapentaenoic acid (EPA) (C20:5 omega-3), the precursor to DHA and the other major dietary omega-3 LCPUFA, can exert similar actions to DHA [50]. There is currently no recommended daily allowance of any fatty acid, but supplement companies suggest somewhere between one to three grams per day.

Carotenoids

Carotenoids are organic pigments synthesised by plants, algae, fungi and some bacteria. They cannot be synthesised by humans or animals, and so have to be consumed. The two types of carotenoids are carotenes (composed entirely of carbon and hydrocarbons) and xanthophylls (contains oxygen atoms).

In humans, four cartenoids (beta-carotene, alpha-carotene, gamma-carotene, and beta-cryptoxanthin) have vitamin A activity, and these and other carotenoids can also act as effective antioxidants. Beta-carotene in particular is able to reduce single oxygen radicals [51].

Certain other xanthophylls (lutein, meso-zeaxanthin and zeaxanthin) form the macular pigment (MP), giving it its characteristic yellow appearance. The largest concentration of lutein and

zeaxanthin lie at the fovea, and reduce with eccentricity [52, 53]. The measurement of MP has recently become the focus of AMD research – some studies have shown those with low MP optical density (MPOD) are at risk of AMD compared with age-matched controls (please see the research in section 1.7, 'Lutein and Zeaxanthin for AMD; a review of evidence').

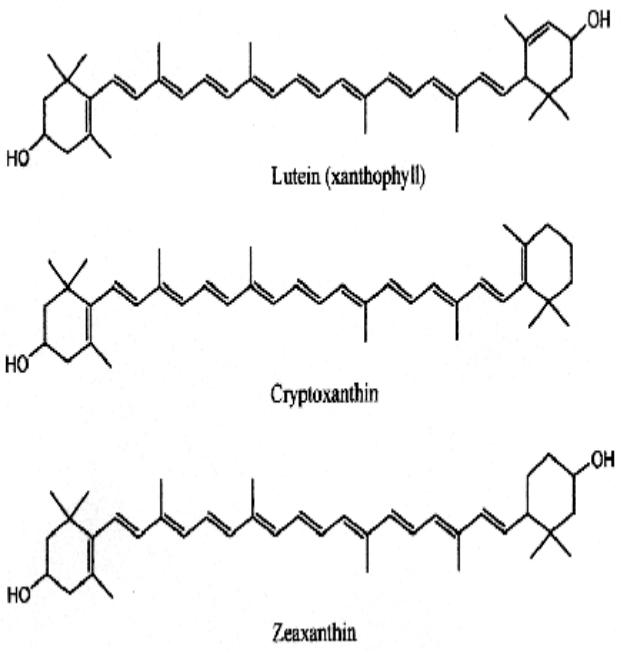


Figure 1.6. Chemical structure of Lutein, cryptoxanthin and zeaxanthin, showing a long straight chain composed of two identical units joined by a double bond between carbon 15 and 15'.

As well as being antioxidants, the xanthopylls act directly to absorb damaging blue and near-ultraviolet light around the 400-460 nm region of the spectrum which would protect the outer retina, RPE and choriocapillaries from oxidative damage [54]. Studies have shown that in rhesus monkeys that have no previous exposure to xanthophylls and no detectable macular pigment, foveal protection has been absent, but became evident after supplementation of the nutrients [55]. The methods used to prevent oxidation are firstly the energy transfer to the carotenoid which will quench singlet oxygen due to the conjugate double bond within their molecular structure, and secondly the reaction with peroxy radicals that are involved in lipid peroxidation.

As mentioned, xanthophylls are not synthesised by the body and can only be obtained from consumption. They are abundant in dark green leafy vegetables such as spinach and kale [56], as well as yellow and orange fruits and vegetables such as peppers [57] (please see **Appendix 5** for lutein and zeaxanthin rich foods). The foremost research into carotenoids in recent years is AREDS in 2002, with the secondary study having been completed in 2013. From these studies,

the current RDA for AMD sufferers or those with an AMD risk is 10mg of lutein and 2 mg of zeaxanthin per day. A comprehensive review of these studies is presented in the next chapter 'Lutein and zeaxanthin: a review of evidence' and section 2.9, 'Clinical intervention of other nutrients'.

Chapter Two

Lutein and zeaxanthin for AMD – a review of evidence

The body of evidence supporting a role in AMD risk and/or progression ranges from basic experimental studies with animals to clinical and epidemiological investigations [58, 59]. Whilst some epidemiological studies suggest a beneficial role for carotenoids in the prevention of AMD, others did not find a relationship. Despite this contradiction, the positive outcomes of many of the studies have given hope that variation of the antioxidant balance through supplementation can slow progression of ARM to AMD [60].

2.1 Search

A search of the research into dietary intake and supplementation of lutein and zeaxanthin was performed from the calendar dates of September 2011 to September 2012 using the following search terms: 'Age-related macular degeneration', 'Nutrition', 'Lutein and zeaxanthin', 'Diet', 'Supplements' on the following databases: Web of Knowledge, The Cochrane Library, Optics Infobase, PubMed, Ovid Journals, PsycArticles, National Center for Biotechnology Information (NCBI) databases, and Wiley Online Library. Since the 'outcome' for much of the research varies – i.e. using visual acuity, retinal signs or macular pigment optical density (the amount of macular pigment within the retina often abbreviated to MPOD) as a standard - studies were included no matter what measure the researcher decided to use. Epidemiological studies were included as well as intervention studies. There were 103 papers that fit the search criteria, and 62 were identified as supplementation or dietary studies in participants with AMD.

Positive findings - observational studies

Firstly, the following research studies found that a diet high in lutein and zeaxanthin effects AMD risk and progression. Moeller *et al's* - Cartenoids in Age-related Eye Disease Study (CAREDS)- research showed that a diet rich in lutein and zeaxanthin in 34 participants with advanced AMD resulted in protective, but statistically non-significant, associations in the overall sample and in women younger than 75 years [54].

Lutein and zeaxanthin has been shown to reduce the risk of acquiring the condition in high risk patients, or slowing progression to an exudative form. The AREDS authors evaluated the relationship of the dietary intake of carotenoids lutein and zeaxanthin, and vitamins A, C and E on 4519 participants using food frequency questionnaires. A higher dietary intake of

lutein/zeaxanthin was independently associated with decreased likelihood of having neovascular AMD, GA, and large or extensive intermediate drusen after all covariates were taken into consideration [61]. This finding was similar to those reported by Lintje Ho *et al.* [62] – participants of the Rotterdam Study (a large population based prospective study that has been on-going since 1990, investigating hepatic, cardiovascular, neurological, ophthalmic, psychiatric, dermatological and oncological diseases) who were calculated to be at risk of developing AMD due to their genetic variants had their dietary intake assessed. Those with high intakes (above the median) of DHA/EPA, zinc, lutein and zeaxanthin all reduced their risk of acquiring early ARM. The Blue Mountains Eye Study [63] assessed the relationship between baseline dietary and supplement intakes of lutein and zeaxanthin, carotene (α and β), β-cryptoxanthin, iron, zinc, lycopene, vitamins A, C and E, and the long term risk of incident AMD. Risk was assessed using logistic models after adjusting for age, smoking, and other risk factors. They found that a higher dietary lutein and zeaxanthin intake reduced the risk of long-term incident AMD, and zinc was also protective if taken both in the diet and supplemented. They were unable to definitively associate reduced risk with the other tested antioxidants.

Lutein and zeaxanthin intake has been found to vary with gender, race and age. Johnson *et al* [64] investigated dietary intake of lutein and zeaxanthin in participants of the National Health and Nutrition Examination Study in 2002 – 2003. The study revealed that amongst all age groups, both sexes, and all ethnicities, intakes of lutein were greater than of zeaxanthin. Relative intake of zeaxanthin to lutein decreased with age, with zeaxanthin to lutein ratios lower in females. Zeaxanthin to lutein ratios in Mexican Americans was considerably greater than other ethnicities. Lower zeaxanthin to lutein ratios were measured in groups at risk for AMD which revealed that the relative intake of lutein and zeaxanthin may be important to AMD risk.

Concentrations of lutein and zeaxanthin can be measured by looking at the serum content in the blood. Delcourt *et al.* [65] in the population based Pathologies Oculaires Liees a l'Age study, measured the plasma levels of lutein and zeaxanthin using high-performance liquid chromatography in 800+ subjects. They found that increased plasma levels of these carotenoids were associated with lower rates of AMD and cataracts, but particularly zeaxanthin seem to play a protective role.

A systematic review and meta-analysis by Ma *et al*. found six cohort studies (van den Langenberg, van Leeuwen, Moeller, Tan, Cho and Cho *et al*.) that positively correlated a high

intake of lutein and zeaxanthin with a reduction of risk in late AMD. None of the six studies found a relationship in early AMD [66].

Positive findings – intervention studies

Lutein and zeaxanthin have been given to participants in supplement form in some studies. Piermarocchi *et al.* - Cartenoids in Age-related Maculopathy Italian Study (CARMIS) [67]- treated 153 patients with AMD and VA of greater than 0.3 LogMAR with lutein, zeaxanthin, astaxanthin, vitamin C, vitamin E, zinc, and copper. Patients received baseline, 6-month, and 1-year follow-up with ETDRS and the 39-item Visual Function Questionnaire (VFQ). After 1 year, treated patients showed stabilization of VA and significantly better ETDRS scores compared to controls. VFQ-39 scores were significantly increased in the treatment group. In the Lutein Antioxidant Supplementation Trial (LAST), patients with atrophic AMD were given 10 mg lutein or 10 mg lutein and other antioxidants over a 12 month period. The authors found lutein combined with other antioxidants to be more effective that just lutein alone, but both groups displayed improved contrast sensitivity, glare recovery and visual acuities [68].

Lui *et al*. conducted a meta-analysis of eight randomly controlled trials (RCT) of lutein and zeaxanthin (Piermarocchi, Bartlett, Richer, Ma, Weigart, Murray, Dawczynski and Beatty *et al*.) They found that xanthophyll carotenoids supplementation was associated with significant improvements in VA and CS in a dose-response relationship. In addition, a linear association was indicated between MPOD increase and the improvement of VA and CS at middle frequency [69].

The foremost and most current research into lutein and zeaxanthin supplementation is the follow up to the original Age-related Eye Disease Study – AREDS 2 [70]. The AREDS team recently released the results for AREDS 2 in which lutein and zeaxanthin was encompassed into the original AREDS supplement formulation [71]. The study found that adding lutein and zeaxanthin did not further reduce the risk of progression to advanced AMD. However, participants who took the AREDS formulation with no beta-carotene but with lutein and zeaxanthin, had their risk of progression to advanced AMD reduced by 18% compared to those participants who took the AREDS formulation that contained beta-carotene but no lutein and zeaxanthin. In addition, participants who had ≤ 0.823 mg per day dietary intake of lutein and zeaxanthin at the start of the study, but who took the AREDS 2 formulation, were 25% less likely to develop advanced AMD compared with participants with similar dietary intake who did

not take the supplementation. There was no benefit from supplementation to those who consumed ≥ 1.030 mg of lutein and zeaxanthin per day in their diet.

Investigators suggested that beta-carotene may have masked the effects of lutein and zeaxanthin in the overall analysis because it competes for absorption in the body – participants who took beta-carotene along with lutein and zeaxanthin had lower serum levels compared with those who only took lutein and zeaxanthin. It can therefore be concluded that lutein and zeaxanthin may be useful substitutes for beta-carotene in the original formulation as beta-carotene has been linked with increased risk of lung cancer in smokers [72]. Leading AMD researchers in the UK have commented on how these results should form the standard of care for all patients with or at risk of AMD [73].

Negative findings – observational studies

Bartlett *et al.* [74] was one of the research teams that investigated diet and supplementation. They conducted a prospective study of 74 patients that were either under 50 years of age, over 50 or over 50 with AMD, investigating their overall diet and supplementation using food diaries over a three-day period. Participants over 50 consumed more vitamin C and fibre than the under 50 group. The AMD group showed no deficiency of any specific nutrient in the diet compared with age and gender matched controls, and consumed more protein and zinc compared to the other groups. The AMD participants consumed more ocular health supplements than the other groups, but the under 50 group consumed more multivitamin supplements, but less dietary vitamin C and fibre.

Another diet study by Cho *et al.* [75] followed patients 50 years of age or over with no diagnosis of ARM or cancer at baseline for up to 18 years for women and up to 12 years for men. Fruit and vegetable intakes were assessed with a validated semi-quantitative food-frequency questionnaire up to five times for women and up to three times for men during follow-up. Fruit intake (especially oranges and bananas) was inversely associated with the risk of neovascular ARM. Participants who consumed three or more servings per day of fruits had a pooled multivariate relative risk of 0.64 compared with those who consumed less than 1.5 servings per day. The results were similar in women and men. However, intakes of vegetables, antioxidant vitamins, or carotenoids were not strongly related to early or neovascular ARM.

Other studies report findings that do not support the association between lutein and zeaxanthin and the reduced risk of AMD [76], or were observed only in population sub-groups [77]. Mares *et al.* [78] did not specifically screen for lutein and zeaxanthin in the diet, but they looked at healthy

diets as a whole, and used the Healthy Eating Index to assign scores to the diets of women who were enrolled in the CARED study. They found that those participants that scored high had a 46% lower risk of early AMD, than those that scored low. The study was limited to those with a high socio-economic status, so the sample was not a true representation of the population.

Because lutein and zeaxanthin make up the MP, studies investigating possible links between MPOD and AMD have been conducted, using a variety of measurement techniques [79]. These will be discussed in the next section.

2.2 Macula pigment and optical density

Some of the MPOD studies have supported an MPOD-AMD association, that is, high values of MPOD mean less risk of developing AMD [80-82] and others have not [83, 84]. Macular pigment optical density measurements, however, can be unreliable. The most common method for measuring MPOD is heterochromatic flicker photometry (HFP), in which an observer is required to 'flicker match' using one wavelength of light that is absorbed by MP and one wavelength of light that is not. Traditional heterochromatic flicker photometry requires the observer to adjust the luminance ratio of the two wavelengths of light at a central macula area and a peripheral area, until the flicker is perceived to disappear or be reduced to a minimum. This can be conceptually difficult to achieve, and as Bartlett *et al* point out, differences in training in the technique provided to participants or by differences in instrumentation can provide differences in reliability [85]. These reliability issues must be taken into consideration when reviewing the following studies.

Studies also show a link between increased intake of lutein and zeaxanthin, and higher MP levels, such as the study by Mares *et al.* (the same research group mentioned previously) where MPOD was measured using HFP in the CARED cohort. They found that MPOD was directly related to dietary intake of lutein and zeaxanthin and even more strongly related to serum concentrations [86]. Other studies have found similar results [87-89].

Supplementation studies report increases in MPOD of between 21 and 57% following lutein and zeaxanthin supplementation in people with healthy eyes. Increases in MPOD of between 24 and 36 % have been reported in people with retinal disease. In the LAST II study, the

authors were interested in investigating those specific characteristics that increase MPOD, to determine why MPOD does not appear to increase despite supplementation in some individuals. Some 90 patients with atrophic AMD were given the same supplementation as the original LAST study, for 12 months, and MPOD was evaluated over that time period. The results showed that MPOD increased with supplementation and decreased slightly without supplementation – those with the lowest MPOD initially, had the highest increase of MPOD [90]. Schalch *et al.* - The Lutein Xanthophyll Eye Accumulation Study (LUXEA) [91]- investigated the effect of a daily lutein and/or zeaxanthin supplement on MPOD as well as blue light sensitivity after 6-12 months use. They found that average xanthophyll plasma concentrations increased up to 27-fold and MPOD increased by 15% upon just lutein or lutein and zeaxanthin supplementation. Supplementation of zeaxanthin alone produced a 14% MPOD increase especially in the parafoveal area. The authors concluded that lutein is predominantly deposited in the fovea, while zeaxanthin deposition appears to cover a wider retinal area.

Bone *et al.* gave their subjects a 120-day supplement regime containing primarily meso-zeaxanthin, but also lutein and zeaxanthin , and measured serum levels and MPOD[92]. Serum levels of all three cartenoids naturally increased during supplementation, and the macular pigment rate of change (measured at 460nm) rose at an average rate of 0.59 mili-absorbance unit/day; which was significantly higher than the placebo group.

However, Berrow *et al.* [93] compared the macular pigment in different age ranges. The findings showed that there was no statistical significance in dietary lutein and zeaxanthin intake between the MPOD of different age groups, and no differences in the macular pigment of the age groups when lutein and zeaxanthin were supplemented in the diet. Another study group found that some subjects failed to show a change in MPOD after their dietary intake of lutein and zeaxanthin was increased [94].

2.3 Clinical Intervention of other nutrients

Zinc

Zinc has often been investigated alongside other nutrients. Of the studies that investigated zinc alone, Newsome *et al* found a positive effect of taking 100 mg of zinc sulphate twice per day for participants with ARM/ AMD of improved visual acuity and fewer drusen compared to the placebo group. However, this study had some limitations since the number of subjects in each

group was relatively small [95]. More recently, Newsome investigated the use of zinc-monocysteine supplementation by prescribing 25mg to dry AMD participants for a period of 6 months. Improvement of visual acuity, contrast sensitivity and macular recovery time in the AMD participants was reported. The investigator did not, however, look at the effect on drusen or other AMD signs such as hyper/hypo pigmentation at the macular [96].

However, Stur *et al.* gave 200mg of zinc sulphate once per day to exudative AMD participants' 'better' eye. The trial showed no short term effect on the progression of AMD in the second eye [97].

Alpha-tocopherol beta-carotene

Male smokers aged over 65 years were given alpha-tocopherol and/or beta carotene supplements for 6 years in Teikari *et al's* study. The authors concluded that both supplements had no effect on the prevalence of AMD or ARM; again, the study had its limitations by not collecting baseline measurements and not using clinical visual parameters [98].

Vitamin Combinations

The Age-related Eye Disease Study (AREDS) [12] is the largest supplementation study of recent years. The team investigated a combination of high dose nutrient supplementation on AMD and cataracts over a period of 6 years. The AREDS formulation of vitamin C 500 mg, vitamin E 400 IU, b-carotene 15 mg, and zinc (zinc oxide 80mg and cupric oxide 2 mg) showed a 25% risk reduction in progression to advanced AMD over 5 years in patients with intermediate AMD (extensive intermediate drusen in one or both eyes, one or more large drusen in at least one eye, or nonsubfoveal geographic atrophy in one eye) or advanced AMD (subfoveal geographic atrophy or choroidal neovascular membrane) in one eye. The risk of losing vision of three or more lines on a Snellen chart also was reduced by 19% with this combination treatment. The AREDS formulation showed no effect in preventing the development of large drusen in participants who had small drusen at baseline, and the incidence of advanced AMD in this group was very low (<1%).

Brantley *et al.* [37] used the original AREDS formulation of supplementation to determine if a short five day course would increase mean plasma levels of oxidative stress biomarkers. They found that the plasma levels of cystine were significantly lower in all participants (AMD and

controls), with no particular differences between the two cohorts. No real differences were found with the other biomarkers however.

It is also not known whether it was one or all of the nutrients working in tandem that gave these positive results in the AREDS study. Because of the high dosage of zinc, and the inclusion of beta-carotene, some ophthalmologists and other eye professionals became concerned with the safety of the formulation for smokers and were reluctant to advise patients to use it. A further study (AREDS 2) [70] was warranted, and it was hoped that the results from this study would give clear guidelines for eye professionals to use. As stated previously, the AREDS team released the results for their follow-up study (AREDS 2) which encompassed lutein and zeaxanthin to the original AREDS supplement formulation [71]. The study found that adding lutein and zeaxanthin did not further reduce the risk of progression to advanced AMD, but because of the large nature of the study, the researchers were not able to measure MPOD and recognise that this would have been a useful dimension to take into consideration. However, as mentioned, the conclusions show that lutein and zeaxanthin may be useful substitutes for beta-carotene in the original formulation as beta-carotene has been linked with increased risk of lung cancer in smokers [72].

To address the risk of lung cancer among smokers supplementing with beta-carotene, Cangemi *et al.* in the Taurine, Omega-3 Fatty Acids, Zinc, Antioxidant, Lutein Study (TOZAL) [72] gave participants with dry AMD a mixture of zinc, taurine, antioxidants (beta-carotene and vitamin A) and Omega-3 for six months. The results showed an increase in VA above the expected baseline decrease in the majority of patients in this population with dry AMD.

Parisi *et al.* [99] – this Italian research group investigated the effect of carotenoid and antioxidant supplementation on retinal function in early AMD patients and age-matched controls using multifocal electroretinograms (a method to record the responses of photoreceptors). Participants were given oral supplementations of vitamins C and E, zinc, copper, lutein, zeaxanthin, and astaxanthin daily for 12 months. Multifocal electroretinograms were assessed initially and, in nonadvanced AMD patients, after six and 12 months. The AMD patients had reduced responses at baseline when compared to the 'normal' cohort, but after six and 12 months of supplementation, central responses significantly increased (but peripheral responses did not).

In 2005, van Leeuwen *et al.* [100] assessed the diets of some of the Rotterdam Study cohort who had been considered 'at risk' of developing AMD by the ophthalmic study group. They found that dietary intake of both vitamin E and zinc was inversely associated with incident AMD. An above-median intake of all four nutrients, beta carotene, vitamin C, vitamin E, and zinc, was associated with a 35% reduced risk of AMD. Exclusion of supplement users did not affect the results. In this study, a high dietary intake of beta carotene, vitamins C and E, and zinc was associated with a substantially reduced risk of AMD in elderly persons.

However, as before, not all the research has yielded positive results. Christen *et al.* [101] tested whether supplementation of vitamin E taken on alternate days, and a daily vitamin C supplement would affect the incidence of AMD diagnosis amongst a male physician cohort who had not been given a AMD diagnosis previously. The supplements were taken over an 8 year period. The researchers found no appreciable beneficial or harmful effect of the supplementation to the risk and therefore diagnosis of AMD.

Overall, due to the negative conclusions of a few of the intervention and MPOD studies, the US Food and Drug Administration and the US National Institutes for Health concluded that the evidence is insufficient to prove that lutein, zeaxanthin and other antioxidants/ vitamins would be beneficial to reduce the risk and progression of AMD and other health conditions [102, 103]. Coleman *et al* dispute this, and hypothesise that if the eight million people in the US who they estimate are at high risk of AMD would take supplement therapy, more than 300,000 of them could be saved from advanced AMD in the next five years [20]. A recent review by Evans and Lawrenson concludes that there is "moderate quality evidence that people with AMD may experience a delay in progression by taking specific antioxidant vitamin and mineral supplements."[104]

2.4 Knowledge and attitudes towards nutrition and supplementation

As shown, there is a growing body of evidence that suggests that consuming antioxidants particularly lutein and zeaxanthin, can have a positive effect on risk of progression, and perhaps onset, of AMD. However, hypothesising aside, expecting people to understand and comply with diet changes can be extremely problematic.

Because of the conflicting research results, neither patients nor practitioners are clear about what kind of supplements to take, or how foods should be prepared and consumed in order to maximise absorption of useful nutrients. To add to the confusion, there are many nutritional supplements aimed at those with AMD currently on the market, with varying degrees of dosage despite the fact that only the AREDS formulation is supported by a large scale randomised controlled trial. Research has shown that given more choices, patients are much more likely to be overwhelmed [105]. Supplements are not regulated in the same manner as medication in the UK [106] and it is very difficult to identify which supplements are likely to be of any benefit.

In a similar way, the information available in newspapers and magazines and on the internet can provide confusing advice as to which are the best dietary sources of lutein and zeaxanthin. For example, the Royal National Institute for the Blind (RNIB) website states that 'Lutein can be found in yellow peppers, mango, bilberries, and green leafy vegetables such as kale, spinach, chard and broccoli' [107]. This statement suggests that all of these foods are good sources of lutein. In fact, as can be seen in **Appendix 5,** the lutein and zeaxanthin content varies in different fruit and vegetables – the difference between 2 mg/cup (mango) and 24 mg/cup (kale).

Marketing can also send out the wrong message to people and practitioners. For example, the drinks manufacturer Rubicon uses the fact that papaya contains lutein to market their juice product. However, papaya juice contains just 0.06 mg lutein per cup. People would have to drink 167 cups of Rubicon papaya juice per day in order to consume 10 mg of lutein.

Other barriers to patients taking preventative measures include poor communication with practitioners, misinformation in the marketplace and age-related compliance problems [105].

Overall, possibly due to the conflict and confusion, recent data suggests that dietary intake of carotenoids have declined in Europe and the US [108, 109]. It is important to investigate the affect that knowledge and attitudes towards nutrition have towards diet and dietary behaviours.

Knowledge and attitudes

Knowledge mediates the relationship between motivation and decision accuracy, and therefore is key to making choices [110]. Nutrition advice is currently available from a vast array of sources – books, the media, old-wives tales, medical practitioners, alternative medicine practitioners, nutrition clubs, support groups, online forums. These sources often convey overly negative

messages or exaggerated good/bad food distinctions [111], (e.g. “Sugar is poison”, “Carbohydrates can make you fat”, “Fat causes heart attacks”) and it can result in unconditional rejection of nutrition guidance by eliciting feelings, such as guilt, anxiety, helplessness, and fear [111]. Many people are not only confused about the ‘correct’ food choices, but are actually fearful and can become obsessed – a new form of eating disorder known as orthorexia [111, 112].

Dr Bressler, who was one of the original AREDS team members, reports that misinformation about supplements is rife in the US, mainly due to the media, well-meaning friends and family, and practitioners [105]. Part of the problem might lie with the plethora of formulations that are available – for example, Bausch & Lomb offers at least six different eye-related vitamins (six versions of Ocuvite and nine versions of PreserVision[105]). This is combined with the fact that many people with AMD are older and may already be taking many drugs, and fundamentally do not understand how medications work. Many individuals feel that taking more vitamins than the recommended dose will not do them any harm [105].

In Germany, 60 pharmacies were contacted to see what advice was being given to AMD patients. Of the 90, 36 of them recommended specific nutritional supplementation, but the supplements recommended were not the AREDS formulation or the correct dosage [113].

The knowledge base of an urban community of mainly older adults in Massachusetts was assessed using a series of surveys in a study by Starkey [114]. A total of 83% of the respondents were aware of a link between healthy food and healthy eyes, but fewer knew of the specific nutrients involved and hence what they should be eating to benefit. Some 40% ate green leafy vegetables three to four days per week, and 73.3% reported that they would take supplements or change eating habits if they knew what supplements to take and which changes to make.

In 1998, a large sample of Irish adults were surveyed for their attitudes towards and beliefs about nutrition and health. The study found significant differences due to several factors: gender (females were more likely to want to eat a healthy diet), education (those with a tertiary education were more motivated to select a healthy diet), and age (younger subjects were less concerned about nutrition than older subjects). Older, more educated, female subjects therefore appear the most motivated to want to eat healthily, but the barrier to this appears to be knowledge on the topic [115].

In fact, the Irish Longitudinal Study on Aging (TILDA) measured the MPOD on subjects from a variety of socio-economic groups. They found that the more educated the subject was, the higher the MP was, and hypothesised that this was due to the knowledge that the subject had of what constituted a healthy diet [116].

Compliance

After their initial study, the AREDS team investigated the compliance of their cohort to their recommendations. Of those participants who met the criteria, only 43% reported taking AREDS vitamins in the recommended dosages. Participants with intermediate or advanced AMD in at least one eye showed a low adherence rate to the AREDS recommendations for vitamin supplementation. Only 59% of all participants reported taking a vitamin supplement for AMD, of whom 71% reported taking an AREDS formulation. Of the 40 participants who met AREDS criteria for vitamin supplementation, 70% reported taking a vitamin supplement for AMD. Of the participants who met AREDS criteria, 43% reported using an AREDS formulation vitamin and were taking the AREDS recommended dosages, 13% were taking an AREDS formulation in quantities less than recommended, 15% were taking a non-AREDS vitamin, and 30% were not taking a vitamin supplement. The six participants who met AREDS criteria for supplementation but were taking a non-AREDS vitamin reported using a vitamin marketed for eye or vision ‘‘health,’’ including two who were taking a lutein supplement. All 17 of the participants taking vitamin supplementation according to AREDS recommendations reported that a retina specialist was the source of recommendation for supplement use. Participants who met AREDS criteria for vitamin supplementation but were taking no vitamin supplement for AMD most commonly reported that vitamin use had never been recommended to them. Other reasons reported for non-use were patients did not think a vitamin would benefit AMD, they were already taking another multivitamin, or they were advised not to take a vitamin by a primary care provider. Their study also shows that lack of awareness of recommendations for supplement use among eligible participants with AMD is a major factor for their non-use of AREDS-type vitamins [117].

A study of 100 patients with advanced AMD conducted at the University of Adelaide found that only 53% were aware of the AREDS supplementation, and only one patient was taking the correct dosage of supplementation [118]. Among those who were aware of the supplement but not taking it, cost was the most common reason, and some were not taking it because of actual

side-effects experienced, fear of potential side-effect and/or fear of interaction with other medications.

Recall of advice is a problem for all age groups, but more so in the elderly. For instance, in one study of smoking cessation with AMD patients, most of the subjects reported never being advised to quit even though their health care providers had records indicating that advice had been given [119].
There is evidence to support poor recall and incomplete adherence to non-pharmacological advice in elderly patients with a variety of medical conditions [120, 121] – not just eye conditions.

Marinac *et al*'s survey into attitudes, use and knowledge of herbal products and dietary supplements [122] found that there were substantial misconceptions among older Americans, and most of the cohort felt that they required significant additional information about these products.

Baker and Wardle's research into fruit and vegetable intake in older adults [123]showed that overall the cohort consumed well below the recommended five-per-day quota. There were gender differences also- men consumed fewer servings of fruit and vegetables compared to women. There were low levels of nutritional knowledge in relation to fruit and vegetables, with men having even poorer knowledge about current dietary requirements and fewer men being aware of associations between diet and disease.

In a Minnesota community, Eikenberry *et al* conducted surveys of low-income subjects to find out their perception, motivations, barriers and promoters of healthy eating [124] . The main motivation for healthy eating amongst higher income subjects was the prevention of disease and for their family; lower income subjects were more concerned with looking good. The barriers to eating healthily appeared to be mainly time, cost and money. Higher income subjects also listed discipline and laziness. Promoters for healthy eating appeared to be family, how the subjects were raised and having a garden and growing produce. Interestingly, most of the subjects had an understanding of the definition of healthy eating (i.e. fruit and vegetables etc.) but did not put this knowledge into practice. [124]

As mentioned formerly, some research has shown that patients with medical conditions that are affected by nutrition, display low compliance with dietary alterations [121]. Reasons why patients might not comply with the evidence include excessive reliance on pharmacological

intervention, lack of knowledge of dietary alterations, disbelief of dietary effectiveness, and ingrained dietary habits[121].

The aforementioned survey of older adults in Massachusetts [114] showed that once the cohort was correctly educated, 75% reported they had changed their eating habits one month later. Although it was not determined what the changes were, it is evident that the value of educational intervention is high.

Overall, knowledge and motivation have been identified as being important for nutrition information processing.

2.5 Complementary Medicine

Supplements that are marketed for ocular conditions are considered to be complementary or alternative medicines and can be sold in pharmacies and health shops. As lutein and zeaxanthin are now 'generally recognised as safe' (GRAS), they can also be added to foods such as cereals.

Eisenberg *et al.*'s 1993 study into US prevalence, cost and usage of complementary medicine showed that expenditure on commercial diet supplements and megavitamins (over the counter) averaged $228 per person per year for diet, $203 for megavitamins yielding national projections of approx. $1.2 billion and $0.8 billion respectively. The study also inferred that a substantial amount of unconventional therapy is used for non-serious medical conditions, health promotion or disease prevention rather than serious medical concerns. However, respondents who reported poor health had higher rates of use of unconventional therapy than those that perceived themselves to be in better health.[125]

Marinac *et al*'s survey into older adults' use of supplements found that Caucasian women in this age group with a college education were most likely to take supplements. Preservation of health was the most predictive indicator for use. Worryingly, primary care physicians generally were unaware of non-prescribed therapies their patients were taking. Most patients did not share this information with their healthcare provider even if they experience adverse effects. [122].

Estimated amount of use in the UK

In 1998, a survey reported substantial use of practitioner-provided complementary/ alternative medicine in the UK, and that 10% of the adult population was estimated to routinely use these medicines over a 12 month period [126]. In 2000, a telephone survey showed that the use of

complementary and alternative medicine in the UK was 20% in the sample [127]. This was predicted to hugely rise due to the aging of the population, the increase in the overall population and the popularity of alternative medicines in Europe [128].

In 2007, research showed that there had indeed been a dramatic increase in sale and use of herbal/ food supplements within UK [129]. This was attributed to a variety of factors including education, media, health-promoting programmes, affluence, fashion trends, type of disease, geography and ultimately public opinion. Individuals who are most likely to use these alternative medicines were identified as young to middle-aged females who are educated and more affluent – especially breast cancer sufferers [129].

Although younger individuals were more likely to use complementary/ alternative medicines, a growing number of older people were beginning to take alternative medicines, but were unsure of the efficacy of drugs that are perceived by some patients as being safe and traditional [129]. The Hertforshire cohort study In 2012 Investigated the patterns of supplement use in a UK population of older adults [130]. 45% of men and 57% of women reported taking at least one supplement in the last three months, and that there were distinct patterns of use which were related to socio-demographic and lifestyle characteristics ; for example, those that were taking oil type supplements (fish oil, omega 3) ate a more unhealthy diet than those that didn't. Those that took glucosamine (or other arthritic supplements) tended to have a higher socio-economic status and a career that consisted of non-physical labour. The researchers hypothesise that in an older age-group, subjects are more concerned with self-medicating or preventing specific diseases rather than general vitamin use for overall health.

In summary, complementary and alternative medicines are being used by the older population, but not necessarily with the correct knowledge of use and dosage. There is a need to educate and inform patients about how best to use such medication.

2.6 Research rationale

Age related macular degeneration is an increasing threat to older adults' sight and quality of life. The current evidence suggests that a consumption of the carotenoids lutein and zeaxanthin – in supplement form or dietary – is likely to help halt the progression of the disease. However, research shows that many individuals with AMD do not consume sufficient quantities of either carotenoid to benefit from these effects.

Due to the conflicting research, poor patient education and poor medical compliance in this age group, it is hypothesised that many patients either do not know about antioxidant intake or are not complying fully. It is vital to find out if this hypothesis is true, so educational dissemination can be studied and intervention strategies can be formed.

It is proposed that a cross-sectional survey should be designed with open ended questions (where appropriate), to find out the knowledge and attitude AMD patients have towards nutrition, and to find out whether their behaviour reflects their attitude.

Use of surveys

Although most survey research is conducted in social sciences fields such as economics and psychology, surveys have been used for many years in healthcare and medicine [131]. They are invaluable in extracting large amounts of important data from a large sample of participants very swiftly, of which the researcher is able to make inference about the wider population.

In healthcare, the advantages of using surveys lie in the non-invasiveness of the research. The participants do not have to undergo any form of treatment or testing in order to find out the answers to specific health questions. Much can be learned from a respondent's attitude, knowledge or behaviour at a point in time, and this can be monitored over a period of time [132]. However, this needs to weighed against the possible low response rates from patients (especially in electronic surveys), and the variety/ bias of responses that occur when a participant is self-reporting. This is of particular note in nutrition surveys, as studies have shown that participants tend to under-report food intake even when novel techniques are used [133, 134]. Both of these drawbacks will be explored in the following chapter.

2.7 Summary

The aim of this thesis is to explore the hypothesis that AMD patients either do not know about antioxidant intake or are not complying fully with supplement use and/or dietary modification. Literature pertaining to L&Z has been reviewed, and a research rationale has been proposed. The following chapter will cover the methods and protocol for the research to be carried out.

Chapter Three

Methods

The previous chapter discussed the literature concerning AMD, nutrition and patient understanding and adherence to medical advice. A research rationale was proposed to explore the attitudes and behaviour in those affected by AMD, with the choice of survey design explained.

3.1 Objectives

The first aim of this project was to design a questionnaire that was effective at assessing attitudes towards, and understanding of, nutrition and nutritional supplementation for AMD amongst people with the condition and amongst age-matched controls. This project was carried out in partnership with the Macular Society. Outcomes of the project include development of educational materials for health professionals, and dissemination of the materials via continuing educational training journals.

3.2 Questionnaire design and validation

A narrative literature review of research on AMD patients' perceptions of nutrition and AMD was conducted from September 2011 to September 2012, using the following databases: Web of Knowledge, The Cochrane Library, Optics Infobase, Ovid Journals, PsycArticles, PubMed, National Center for Biotechnology Information (NCBI) databases, and Wiley Online Library. The following key terms were used: 'Age-related macular degeneration', 'Nutrition', 'Survey', 'Attitudes', 'Behaviours', and 'Diet'. Although there were studies that fitted into the search criteria, this review did not identify any existing measure of AMD patients' perceptions of nutrition, but found most surveys looked at nutritional behaviours. Therefore an original survey was developed afresh. A cross sectional survey was deemed most appropriate to elicit observational data at one specific time; designed with open and closed questions. After discussion with the Macular Society, it was decided that it was important to try and keep participants' answers as 'pure' as possible by not biasing their opinions, and allowing them freedom to express themselves in their own words.

The survey covered three main areas:

1. Demographics: i.e. what are the characteristics of the participant being interviewed? Questions included age, gender, living arrangements, occupation, AMD type and duration, vision impairment registration and health/vision perceptions.
2. Knowledge of AMD patients (or age-matched controls): i.e. what does the participant know about nutrition and the eye, where have they got their information from and do they feel is it enough information for their needs? Questions include whether the participant has discussed supplements with a health professional, do they feel they have enough information, where has that information come from, do they feel specific foods affect eye/general health, do they believe AMD can be affected by nutrition, whether they take any supplements and their beliefs about consumption of specific vegetables and fruits linked to eye health.
3. Diet of participants: i.e. what are participants actually eating? Questions include frequency of vegetables eaten, a 24 hour food diary, who cooks/ prepares food, preventions to cooking/ preparing food, who food shops, where do they shop for food, barriers to changing diets, and supplements and dosage.

The items included in the survey were:

- Age
- Gender
- Living arrangements
- Occupation
- General health
- Visual health
- Confirmation of AMD with duration and type
- Visual impairment register details
- Who mostly prepares food?
- Who mostly cooks food?
- Preventions to preparing and cooking food
- Confirmation of ability to cook a hot meal alone
- Who mostly food shops?
- Where the food is mostly obtained from?
- The most important factor that dictates what food is eaten

- Would the participant like to change diet?
- Preventions to dietary change
- 24 hour food diary, split up into breakfast, lunch, dinner and snacks
- If vegetables were eaten in the previous 24 hours, were they mostly cooked or raw?
- Agreement/ disagreement with a statement that foods can affect general health
- Agreement/ disagreement with a statement that foods can affect visual health
- List of fruits and vegetables that may be beneficial for eye health – participant to say if they agree/ disagree and why
- Which vegetables were eaten in the preceding week
- Has nutritional supplementation been discussed by a health professional
- Are nutritional supplements taken (if not, why)
- Which supplements are taken and how often
- How much money for supplements would participants be willing to pay
- Agreement/ disagreement with a statement that AMD patients are given enough information on how their lifestyle affects their eye health.
- Where have participants received information on AMD from
- Do participants believe that age related macular degeneration can be prevented by lifestyle changes?

3.3 Diet

Food frequency questionnaires (FFQs) have often been used instead of food diaries in nutrition research – the debate over which is more reliable has not been resolved. Many studies show FFQs are useful for foods eaten frequently but not so useful for foods that are eaten infrequently [135]. Some studies have shown there is less measurement error in food recording than in food frequency questionnaires, and the ability to study associations between diet and chronic diseases is slightly easier with food diaries [74, 136]. In one study, 24 hour food recall interviews were shown to overestimate energy and nutrient intakes [137] but were much more accurate than a written food diary in other studies [138]. It was decided that despite the drawbacks seen in some studies, a 24 hour food recall would be the most appropriate method of assessing the participant's diet.

3.4 Survey piloting

The survey was piloted with eight AMD patients who were members of the Macular Society and volunteered to take part. These volunteers formed a focus group to test the reliability, clarity, and understanding among an informed population. This 'face validity' (i.e., does the questionnaire measure what it intends to measure), was the only means of validation that it was possible to perform, due to a lack of other instruments to compare the results with. The focus group had a guided informal discussion structured by a moderator (RS) – the survey questions were asked again to check if the answers matched, and then the volunteers were asked to comment on how easy the questions were to understand and their opinions on the topics covered. The meeting was recorded and analysed to further refine the survey, which was altered accordingly –

1) the type of AMD were made simpler for participants to understand by categorising it 'wet' or 'dry'

2) adding a 'meals-on-wheels' category as to where participants might have obtained food from

3) adding 'more information' if the participant was having trouble understanding a question, which would allow the interviewer to clarify without biasing the answer.

Please see a transcript of the meeting in **Appendix 6.** The final survey (see **Appendix 7**) was then administered to future participants.

Because of the age group and visual impairment of the participants, it was decided it would be best to deliver the questionnaire verbally. It was not practical to administer a verbal questionnaire face-to-face, as participants live across the country, so a telephone interview was conducted instead. In order to keep all the information in one place, survey software was used by interviewers to record the results. Bristol Online Surveys was the software used (University of Bristol, 8-10 Berkeley Square, Bristol BS8 1HH, UK). The survey was created with 'branches' that would appear/disappear according to what was answered, so that an interviewer did not have to record 'not applicable' to inappropriate questions.

3.5 Sample size

The sample size required for questionnaire studies can be estimated by using a sample size chart. There are roughly 500,000 people with AMD in the UK. In order to be 95% confident that our sample represents the UK AMD patient population, we would need to recruit 383 subjects with AMD. To represent the number of Macular Society members (approximately 16000+), we would need to recruit 370 subjects. When compared to other surveys, however, both of these figures are unrealistic due to the amount of data that is collected. Using data from a previous study from Bartlett *et al.* [74], a minimum sample size of 96, confidence interval of 10 and a confidence level of 95% would be appropriate.

3.6 Recruitment

The Macular Society is the only UK charity that is dedicated to helping those with diseases of the macula. They provide impartial information and practical support for visually impaired people, their families and carers. They also "provide information for health professionals, campaign for better services, sponsor research and raise awareness of macular degeneration and preventative measures" [139]. Because of their work and dedication to improving education to patients, we approached the Chief and Chief executive to ask for assistance with recruitment with a mutual sharing of results. Patients that rang the society helpline over a period of time (January 2012 – May 2012) were invited to take part in the study, in a 'first come, first served' basis. However, by March 2012, there were sufficient numbers of participants and recruitment finished early.

Four Macular Society workers administered the questionnaire. They were given extensive written instructions on how to administer the questionnaire by asking the questions exactly as they were written (see final survey in **Appendix 7**), with no emphasis on any word and no promptings. For the questions that required greater clarification, an 'additional information' tab was included, which the worker could then read out. The workers listened in to at least two mock interviews and had the chance to pilot the questionnaire on themselves. The workers were able to contact the principle investigator and supervisor for any help they required (however, none did).

2.7 Inclusion/exclusion criterion

The inclusion criteria were that participants should be aged over 55 and have been diagnosed with a form of AMD. The only exclusion criterion was the inability to hear and reply to questions in English over the telephone.

3.8 Ethics

This study was conducted according to the guidelines laid in the Declaration of Helsinki and all procedures involving human subjects were approved by the Aston University Ethics Committee. Verbal informed consent was obtained from all subjects and formally recorded.

3.9 Questionnaire delivery protocol

When a patient agreed to take part in the study, they were telephoned at a convenient time to complete the questionnaire. Information about the study and a consent statement was read out to each participant at the start of the follow-up call, before the questionnaire was delivered. The participants had the opportunity to ask questions about the study at recruitment and when they were called by the interviewer.

Summary of telephone interview protocol:

1. Introduction and confirmation that the participant is willing to participate at that time
2. Arrangement of an alternative interview time if required
3. Withdrawal from the study if required
4. Study information read out to the participant
5. Consent statements read out to the participant and consent confirmed
6. Questionnaire delivered and responses recorded
7. Participant given the opportunity to ask questions
8. Participant provided with contact numbers in case any questions arise later
9. Telephone interview is ended.

Participants had the opportunity to ask questions about nutrition for eye health that may have been prompted by the questionnaire at the end of the interview –if they felt they required written material they were posted a leaflet with diet and nutritional supplement information.

They were also given a contact number if they thought of any questions after the interview ended, and one participant called for advice regarding supplements at a later date.

3.10 Analysis

Microsoft Excel (Microsoft Thames Valley Park, Reading, West Berkshire RG6 1WA) was used to perform initial analysis; quantitative data was summarised using percentages and graphs.
The data from the diet based question ("What did you eat yesterday?") was entered into dietary analysis software 'A La Calc' (Red Hot Rails LLP, Unit 9, Eurolink Business Park, Middle Bank, Doncaster, South Yorkshire. DN4 5JJ). Each participant's food was entered into the software as a 'recipe', which allowed the software to then analyse calorific intake, nutritional characteristics and most essential nutrients, including lutein and zeaxanthin. All these details were exported into Excel for further analysis.

Data from Excel was then used in statistical software IBM SPSS to draw comparisons between people with and without AMD, using T-tests or Chi-squared analysis in the case of categorical data. For example, an independent t-test was used to compare the ages of participants in each group. Pivot tables were used to summarise the data and for cross-tabulation. Qualitative data was grouped into categories and general themes were extracted to then use in SPSS.

3.11 Conclusion

In this chapter the methods and protocols employed to design, validate and deploy a nutritional survey for patients with age-related macular degeneration have been discussed. In the following chapter the results that were obtained from the survey in participants with AMD, and an age-matched control cohort will be described.

Chapter Four

Age-related macular degeneration patients' awareness of nutritional factors.

This chapter has been published in the British Journal of Visual Impairment [140] See Appendix 15 for a copy.

The previous chapter outlined the methods and protocol in delivering a cross-sectional qualitative survey to patients with and without AMD. In this chapter, some of the data and demographic results from the survey will be described.

4.1 Introduction

Age-related macular degeneration (AMD) is the leading cause of visual impairment in older adults (> 50 years) in the UK [5]. Currently, there are several AMD classification schemes which have been developed to try to standardise research and clinical practice. Ferris et al.[11], proposed a five stage classification scale in which the investigators claim some consensus among AMD specialists: Stage 1) No apparent aging changes, 2) Normal aging changes, known as 'drupelets' (small drusen ≤63 μm) 3) Early AMD – medium sized drusen ≤125μm 4) Intermediate AMD - large drusen and pigmentary (hyper or hypo) anomalies and 5) Late AMD – geographic atrophy and/or neovascularisation [11]. AMD can cause a gradual loss of central visual function occurring within months, or over many years, and late AMD can cause central visual loss and metamorphopsia within days or even hours. Many AMD patients have been given a simplified classification using the terms 'dry' to describe geographic atrophy and 'wet' to describe neovascularisation or exudation. Visual loss is strongly associated with a reduction in quality of life as it will limit the ability to perform daily activities. Subsequently, depression often occurs in these patients [141]. It has been predicted that the prevalence of AMD will increase significantly by 2020 due to the generalised aging of the population [15, 16], but also due to socio-economic factors such as poor nutrition and increased smoking in some areas [142, 143]. Therefore it can be expected that there will be a growing need for support services for people with this condition.

In the UK, diagnosis for AMD occurs via an ophthalmologist [5]. Often, after the initial diagnosis, the patient will receive written information regarding the disease from the ophthalmology

department. The decision then rests with the ophthalmologist as to whether the patient requires any treatment. This might take the form of anti-vascular endothelial growth factor medications (e.g. Lucentis®) or surgery/laser for wet AMD conditions, low vision services or placement upon a sight impairment register. If the AMD is of an early or intermediate stage, the patient will have very little contact with any hospital services for some years – if at all – unless the AMD changes to a late stage. Patients are advised to have a yearly eye examination with an optometrist who will monitor the condition, but is often unable to provide physical or psychological help without referral [13].

Whilst specialists agree that smoking has an impact on AMD and that cessation will halt progression of the disease [119], there are conflicting research findings and therefore conflicting information provided by eye care practitioners regarding the impact of nutrition on AMD [105].

The Age-Related Eye Disease Study reported that nutritional supplementation in people with intermediate AMD can reduce their risk of progression to advanced AMD by 25 % [12]. While the AREDS was in progress, evidence emerged to suggest that the dietary nutrients lutein and zeaxanthin may be more effective than other nutrients in reducing AMD risk or progression due to their antioxidant and photo protective properties [144]. The plausibility for this hypothesis is due to the high concentration of lutein, zeaxanthin, and a related compound meso-zeaxanthin, in the macula, particularly in the fovea, which form the MP [145]. The protective properties of the MP are now well established and include the ability to interact with free radicals, prevent lipid peroxidation and filter out incoming, high energy blue light [146 39 147 5]. Some studies also show a link between increased intake of lutein and zeaxanthin, and higher MP levels [89 87 148]. Supplementation studies report increases in macular pigment of between 21 and 57% following lutein and zeaxanthin supplementation in people with healthy eyes. Increases in macular pigment of between 24% and 36% have been reported in people with retinal disease. One randomized controlled trial reported an improvement in several measures of visual function in a group of veterans who supplemented with 10 mg of lutein for one year [68 113].

A recent study by Loughman et al. [149] suggests that supplementation with all three macular carotenoids may offer advantages both in terms **of** macular pigment optical density (MPOD) response and visual performance enhancement. The AREDS team recently released the results for their follow-up study (AREDS 2) which encompassed lutein and zeaxanthin to the original AREDS supplement formulation [150]. The study found that adding lutein and zeaxanthin did not further reduce the risk of progression to advanced AMD. However, investigators report that lutein and zeaxanthin may be useful substitutes for beta-carotene in the original

formulation [72]. Despite the conflicts, overall, the research evidence suggests that high macular pigment levels could reduce risk for onset or progression of AMD.

Because carotenoids are not synthesised by the human body, they have to be acquired either in the diet or by supplementation. Research shows that the highest mole percentage of lutein and zeaxanthin are in egg yolk, maize (corn), spinach, collard greens (like cabbage) and kale [151] [152]. Maize has been identified as the vegetable with the highest quantity of lutein and orange pepper was the vegetable with the highest amount of zeaxanthin. Amounts of lutein and zeaxanthin are also reported to be present in kiwi fruit, grapes, orange juice, courgettes, and different kinds of squash. Predominantly, leafy green vegetables have a highest content of lutein and zeaxanthin.

Despite the body of evidence in support of a role for dietary modification or nutritional supplementation in reducing risk of progression of AMD, neither patients nor practitioners are clear about what kind of supplements to take, or how foods should be prepared and consumed in order to maximise absorption of useful nutrients [105]. To add to the confusion, there are many nutritional supplements aimed at those with AMD currently on the market, with varying degrees of dosage and some without any research basis at all [153] [149]. Many do not contain the AREDS formulation. Research has shown that given more choices, patients are much more likely to be overwhelmed [105]. Supplements are not regulated in the same manner as medication in the UK [106] and it is very difficult to identify which supplements are likely to be of any benefit.

Since many local authorities do not have standardised rehabilitation services in place [154], some patients have been turning to non-professional charities, such as The Macular Society, to acquire information and support. The Macular Society is the only national UK charity that is dedicated solely to helping those with diseases of the macula. The Macular Society provide impartial information and practical support for visually impaired people, their families and carers. They also “provide information for health professionals, campaign for better services, sponsor research and raise awareness of macular degeneration and preventative measures” [139].

The objectives of this study were firstly to find out who pursues the help of a non-professional charity, and secondly, to determine the beliefs and understanding that these AMD patients have about the impact of nutrition on the condition, and where patients have obtained information about nutrition.

4.2 Methods

Participants

A total of 158 participants were recruited between January 2012 and March 2012. Recruitment was via the Macular Society helpline volunteer worker. Patients aged over 55 years of age who contacted the Macular Society helpline between January 2012 and March 2012 were asked if they would like to take part in a telephone survey (once they had received all the assistance they needed from the Macular Society). Pre-requisites for potential participants were that they should be aged over 55 years and have been diagnosed with a form of AMD; exclusion criteria were the inability to hear and reply to questions in English over the telephone. No attempt was made to define and categorise the amount of visual loss the participant had, as the objective was to assess typical patients seeking the Macular Society services.

Ethics

The procedures followed were in accordance with the ethical standards of the Aston University Ethics Committee on human experimentation that conform to the Declaration of Helsinki 1975, revised Hong Kong 1989.

Survey Design

A literature review of research on AMD patient's perceptions of nutrition and AMD was conducted of the following databases: Web of Knowledge, The Cochrane Library, Optics Infobase, Ovid Journals, PsycArticles, PubMed, NCBI databases and Wiley Online Library. The following key-terms were used: "Age-related macular degeneration", "Nutrition", "Survey", "Attitudes", "Behaviours" and "Diet". This review did not identify any existing measure of patient's perceptions of nutrition, but found most surveys looked at nutritional behaviours [155]. As a result, a 36 question cross sectional survey was designed to explore nutritional habits, supplement usage, physical abilities in food preparation and cooking, and sources of knowledge in order to ascertain the beliefs AMD patients have, and compare their beliefs with their behaviours. Because the survey was exploratory, it was designed mainly with open ended questions in order to ensure responses reflected participants' true beliefs. In addition, some closed ended questions were included with response scales to grade participants' feelings.

The survey was then piloted on eight AMD participants, from the Macular Society, to test the reliability, comprehensibility, and understanding among an informed population. This 'face

validity' (i.e., does the questionnaire appear correct at face value) was the only means of validation that it was possible to perform, due to a lack of other instruments to compare the results with. Initially, the eight patients completed the survey via a telephone interview. Three weeks later, the patients attended a focus group that had two parts: firstly, the participants completed the survey once more. Next, the participants had a recorded, guided informal discussion structured by a moderator – the volunteers were asked to comment on how easy the questions were to understand and opinions on the topics covered. The results of this meeting were analysed to further refine the survey, which was altered accordingly (e.g. the terms 'wet' and 'dry were employed to coincide with many patient's understanding of AMD classification, extra options were added to some questions, some questions were removed or re-worded and additional instructions were added). The final survey (see **Appendix 7**.) was then administered to the cohort.

The initial questions covered demographic topics such as gender, age, employment, social history, type and length of time with AMD and visual impairment registration. Opinions on diet and supplementation were obtained, with particular interest in whether participants could identify lutein and zeaxanthin rich foods (e.g. kale) amongst other vegetables. Participants were also asked where they had acquired any information about the condition from (for instance, an ophthalmologist, optician, Macular Society). The questions subsequently focused on perceived state of vision and health, and ability to perform preparation and cooking of food. Participants also provided a food diary for 24 hours, as studies have shown there is less measurement error in food recording than in food frequency questionnaires, and the ability to study associations between diet and chronic diseases is slightly easier with food diaries [74 136]. The results of the questions relating to cooking abilities, perceived health and vision states and the food diary is beyond the scope of this paper and will be discussed in a future paper.

Procedure

If a patient agreed to take part, their name and contact details were taken by the helpline worker. The potential participants were read an information factsheet informing them what the survey would involve, how long it would take and how the information would be stored. If the patient decided to participate, an oral informed consent was obtained over the telephone and they were advised that they could withdraw at any time. Usually an appointment was scheduled for a future telephone interview or the interview began immediately if the patient wished.

They were then contacted at a convenient time by one of four Macular Society employees who administered the telephone interview and filled in the survey online at the same time (Bristol Online Surveys). The telephone interview lasted approximately 25 minutes, and was not recorded. Each volunteer was trained (by RS) to ask the questions only, without bias, and if the participant had any questions regarding the survey, they were given the author's contact details, although no participant made any contact.

Data Analysis

The results were analysed to find the mean, median and standard deviation using the software Microsoft Excel. Data from Excel was then used to create charts, and used in statistical software IBM SPSS (version 20) to draw comparisons between supplement cost and usage using chi-square statistics. Qualitative data was grouped into categories and general themes were extracted to then use in SPSS.

4.3 Results

Sample Characteristics

Table 4.1 shows the demographic characteristics of the sample. The gender distribution of the 158 participants showed that there were significantly more females (61%) in the sample than males (39%) (Chi-square p= 0.05). The participants ranged in age from 56 to 95 years; the median age was 80 years. There was a nearly even split between 'wet' (47%) and 'dry' types of AMD (49%), with a small percentage of participants who were unsure of their AMD classification. The median duration of having the condition was 5 years, ranging from 1 to 25 years. The majority of participants lived in their own home – either rented, mortgaged or owned outright, and participants mainly either lived with their partner or alone. The majority of participants were not registered partially sighted or blind, although there was a trend for those participants that had the condition for longer to be on a register (Kruskal Wallis H p= 0.09).

Characteristic		Percentage of Participants
Living Arrangements	Own home	88%
	With family/friends	3%
	Sheltered accommodation	7%
	Other	2%
With	Partner	50%
	Alone	47%
	Other family members	4%
Registration	Blind	16%
	Partially sighted	21%
	None	63%
Supplement price	No cost	17%
willing to pay	£1-5	10%
	£6-10	21%
	£11-15	24%
	£16-20	12%
	£20+	17%

Table 4.1. Demographic characteristics of participants.

Patient's perceptions of diet and eye health

When asked their overall opinions on diet and health, 87% of participants believe that diet affects general health, and 68% believe that diet affects eye health.

Figure 4.1 shows the beliefs that participants held about specific foods:- leafy green vegetables, which are good sources of lutein and zeaxanthin, other fruit and vegetables, and dairy products . Participants were asked if they believed each food was beneficial for eye health, and if they answered 'Yes', they were asked why they thought so.

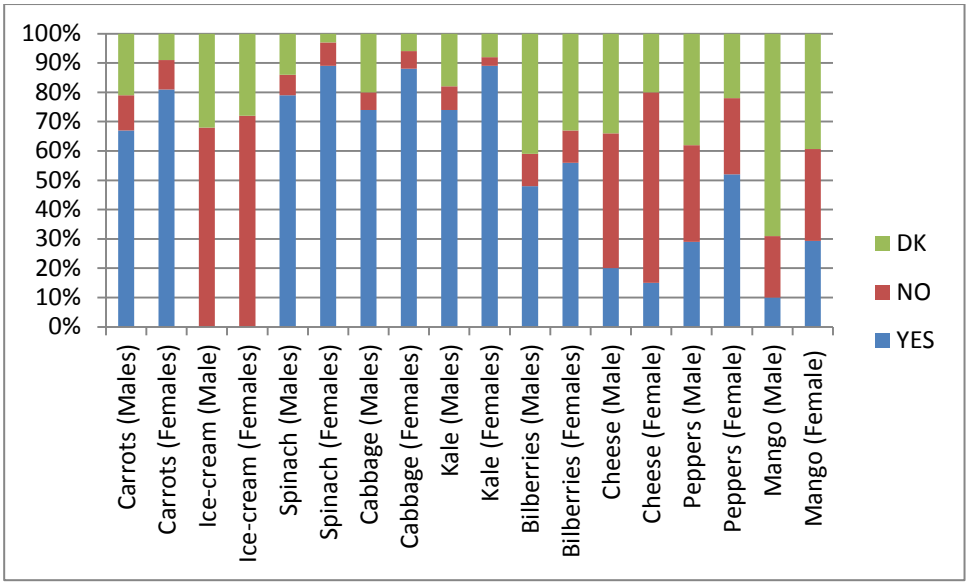


Figure 4.1. Participant's beliefs about the eye health benefits of several foods. 'Yes' indicates the participant believed the food was beneficial, 'No' indicates the participant did not believe that the food was beneficial, and 'DK' indicates the participant didn't know.

As shown, the majority of participants were accurate in their perceptions of the food which would be beneficial for eye health. Leafy green vegetables such as spinach, cabbage and kale were identified as being beneficial by over 80% of participants. Ice-cream was identified as not beneficial for eye health by 72% of participants. For mango, bilberries and peppers, 25% or more participants answered 'don't know', and responses were more mixed. Males responded with 'Don't know' on average 10% more than females.

When asked why they felt a particular food was valuable for eye health, the majority of participants (81%) struggled to verbalise why they held that belief. Of those that did express the reasoning behind their beliefs, the majority of the responses had nothing to do with nutrients. Only 2% of those that felt spinach and kale are beneficial for eye health knew that they contain lutein. Some participants responded that leafy green vegetables were known to be good for eyes (spinach 5%, kale 3%, and cabbage, 6%), while others merely responded that coloured foods were good for eyes (carrots 2%, peppers 5%, and mango 1%). Some participants (1%) responded that spinach and kale contained iron, which was why they felt it would be beneficial for eye health. One percent of participants felt that carrots were beneficial because they contained carotene, and that peppers were beneficial because they contained vitamin C. Participants also included the following reasons for carrots: "They help you see in the dark" (6%), "war propaganda" (6%), "We were told to eat them by parents" (6%). One percent of participants responded that their optician had told them that mango was good for

eye health. Participants also responded that they had “read it was beneficial somewhere” for some foods (peppers 1%, bilberries 5%).

No participant felt that ice-cream was beneficial for eye health. Of the participants that felt that cheese was beneficial for eye health (18%), none could give a reason why.

Nutritional supplementation

The participants were asked who they had discussed nutritional supplementation with - 30% of the participants had discussed it with their ophthalmologist, 15% with their optometrist and 8% had consulted their GP.

Participants were asked if they currently took a nutritional supplement(s). Of those that responded ‘yes’ (79%; of males and 79% of females), the majority (60%) took the supplement once per day. The most popular brand of ocular supplement used was I-caps by Alcon (24%), followed by PreserVision by Bausch&Lomb (19%), Ocuvite by Bausch&Lomb (14%), Viteyes (14%), Macushield by Macuvision (11%), Retinex by Healthspan (8%), Visionace by Vitabiotics (5%), and Vitalux by Novartis (3%). Some patients took more than one brand with a variety of dosing methods.

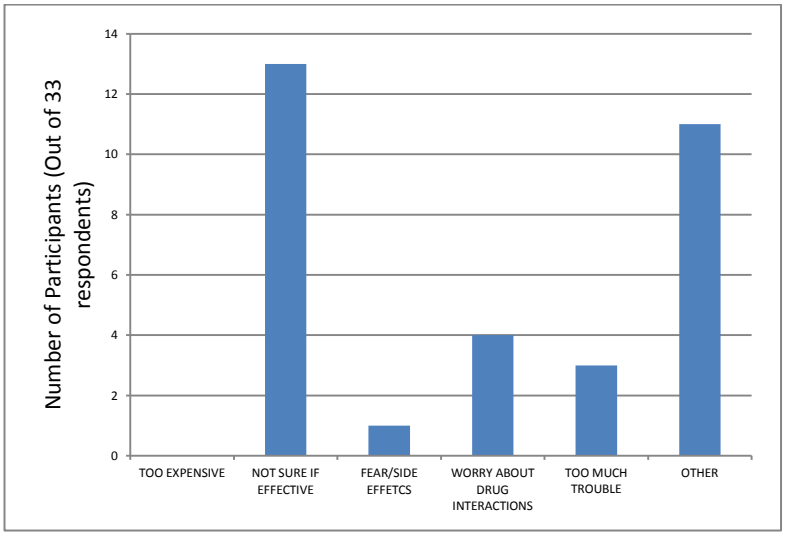


Figure 4.2 . Reasons for not taking Nutritional Supplements.

Those that responded that they did not take a nutritional supplement (33 participants - 21% male and 21% female) were asked to describe these reasons as shown in **Figure 3.2.** The majority felt that they were not sure of the effectiveness of supplementation, but many listed an

'other' reason for not taking supplements (but did not provide an explanation for what that reason might be).

The participants were asked how much money would they be willing to spend on a supplement (per month or 30 day's supply) if they had proof of its worth. The results are shown in **Table 1**. The supplement usage data were cross-tabulated with the amount of money participants were willing to spend on a monthly supplement, using chi-square statistics. The results show a significant association between those that do take supplements being willing to spend more money on supplements, and those that do not take supplements are willing to spend less money on supplementation ($p \leq 0.000$). Of the participants that did not take supplements, 67% were not willing to spend any money on supplementation even if they had proof of its worth.

Patient information

Figure 4.3 displays the opinions that the participants held about AMD and living with the condition. Over half the participants (51%) believed that AMD patients do not receive enough information about nutrition and lifestyle choices; an additional 12% strongly believed this. The participants were asked where they had received information on AMD from – (they were allowed to pick more than one option): 40% of participants had received information from their ophthalmologist. As expected, 92% had received information from organisations such as The Macular Society. Just over half of the cohort believed that AMD could be prevented by lifestyle choices such as nutrition.

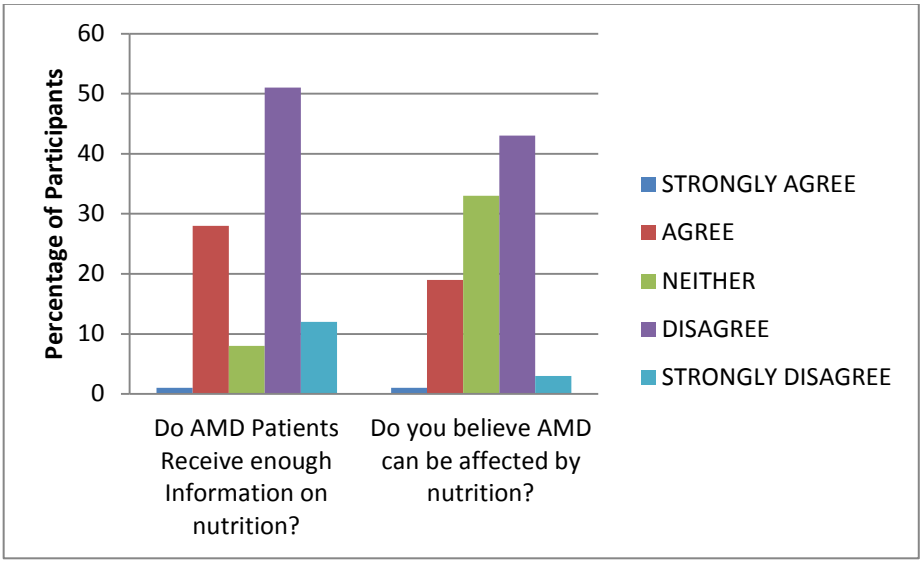


Figure 4.3. Knowledge of AMD

4.4 Discussion

The demographic data has shown three interesting findings:

Firstly, research has shown that females (especially in this age-group) are more likely to ask for and utilise health care services [156] [157], so it could be speculated that more females than males seek out the services of the Macular Society.

Secondly, only 37% of the participants were registered on a visual impairment register, despite 47% of participants having 'wet' AMD (although this was self-reporting and the severity was not assessed). The Royal National Institute of the Blind (RNIB)'s survey into certification and registration in 2011 [158], shows a steady decline in the number of registrations per year despite the fact that the prevalence of visual impairment is increasing [16] [5]. They attribute this decrease in registration not to a lack of interest in registration by the patient, but rather to the length of time it takes to complete the Certificate of Visual Impairment (CVI) by the professionals involved.

Finally, nearly half the participants lived alone – this can have a huge impact on their quality of life. One study [159] has shown that 63% of all blind and partially sighted people live alone – a higher figure than the 'normal' sighted elderly population. It would have been useful to find out if participants had a mobility issue, as this may have affected why the participants had chosen to seek the Macular Society's services – a helpline is easier to access than physically going to see an ophthalmologist or optometrist for advice, and this could explain why patients did not report sourcing their information from an ophthalmologist or optometrist.

The cohort was a group of highly motivated individuals who had taken the initiative to contact the Macular Society but still felt that they needed more advice, particularly relating to nutrition. Although some of the participants needed to rely on others for support and felt they had considerable visual impairment, the desire to remain independent and improve their vision is evidenced through seeking the services of the Macular Society, and using other healthcare professionals such as dieticians and specialist doctors.

This sample may not represent all patients seeking services from organisations like the Macular Society. Access to other organisations would provide a more rounded view. It would be important to find out the opinions of those with AMD who have not sought support from non-professional organisations, and this will form the next step to the overall project.

Patient's perceptions

This study provides a clear picture of the perceptions of diet and eye health among a sample of AMD patients. The majority of participants agreed that specific foods can affect general health, and participants also agreed that specific foods affect eye health. The results of the specific food questions show that the majority of participants felt that the vegetables and fruit were beneficial for eye health, and these perceptions were generally accurate. However, apart from a few individuals who mentioned specific nutrients in regard to specific foods (e.g., lutein in kale), most participants were not able to identify why these foods helped promote eye health, or gave vague responses such as "I read it somewhere". This suggests that participants, who would be expected to be well-informed, were not clear about the links between diet and eye health.

Information

The majority of participants reported that they did not have enough information on nutrition and its relationship to AMD. As expected, all participants reported that they had received information from organisations such as the Macular Society. In contrast, not all the participants reported getting information from their ophthalmologist, which is consistent with previous studies [160] [161]. The data reported here shows that there are clear gaps in the knowledge patients have of AMD risk factors [162]. A lack of information might also explain why four percent of the participants were not sure what type of AMD they were suffering from. Patients appear to be actively seeking advice but not all are getting it from sources such as ophthalmologists or optometrists. These findings are similar to results from the Royal College of Ophthalmologists audit of AMD services in March 2009 [163] which found that there was an insufficiency of resources to deliver adequate AMD Services. Evan and Lawrenson's survey (2012) of eye professionals [164] showed that although over 60% of respondents reported that they frequently provide dietary and supplement advice to patients with established AMD and those at risk of AMD, the nutritional advice given only consisted of leafy green vegetables and oily fish recommendations, and type of supplement recommended did not comply with current best research evidence, based on the findings of the Age-Related Eye Disease Study (AREDS). Only one in three optometrists regularly assessed smoking status and advised on smoking cessation [164]. The results reported in the present study reinforce those of the survey and the Royal College of Ophthalmologists, and provide further evidence that greater support and information provision for AMD patients is needed.

Nutritional supplementation

Over 75% of participants reported taking a nutritional supplement (mainly on a once-per-day basis) – this is a larger number than other studies into supplement usage have found [165] [74] [130] . The majority of patients that were taking ocular supplements were not taking an exact AREDS formulation, and were taking an incorrect dosage or combining it with one or two other brands with the same formulation (maybe believing that more might be better). This pattern of supplementation could reflect a lack of information from healthcare professionals, with only a third of patients having discussed nutritional supplementation with their ophthalmologist, while some participants had not discussed supplementation with anyone at all. Those participants in our study that reported not taking any supplements listed the primary reason as not believing they would be effective, and hence were unwilling to spend much money on an unproven supplement. The high number of nutritional supplements marketed towards people with AMD makes it difficult for both patients and health professionals to navigate this issue for the prevention or treatment of the condition [105].

There are currently no clear supplement guidelines for health professionals to use; The College of Optometrists advises that patients should eat a healthy diet and to stop smoking, adding that there "is no definitive scientific evidence of the effectiveness of nutritional supplements", but patients should speak to their optometrist for supplement advice [166]. Some institutions might have been waiting for the results of AREDS 2, but since the AREDS 2 results have been released, there is a need for unified guidelines for all health professionals. When asked how much participants would be willing to pay for an effective nutritional supplement, only one quarter responded that they would pay more than £11 per month, and there was a significant correlation between those who did not take supplements and those that were not willing to spend any money on supplements.

In conclusion

The development of this survey has created a new measure that can be used again. The study has identified that AMD patients have a definite lack of information and understanding of the link between AMD and nutrition, and this needs to be corrected. The results of this study will inform the design of more effective education and dissemination methods, and help to outline guidelines for health professionals.

Chapter Five

Dietary analysis and nutritional behaviour in people with and without age-related macular disease

A paper published in Clinical Nutrition E-SPEN [167] See Appendix 16 for a copy.

The previous chapter showed the demographic results from the survey. This chapter will present the remaining data and results yielded from the survey. To draw comparisons with people without AMD in this age group, a control group of 50 non-AMD participants were recruited from a group of independent optometric practices across the UK, as well as from Aston University Clinics. Six optometric practices (apart from Aston Clinics) from a variety of areas agreed to take part in recruitment. They were provided with posters advertising the project, information sheets for the patients, and consent forms. If a patient agreed to take part, their contact details were recorded and emailed to the researcher, together with a convenient time, and the questionnaire would be administered. All patients, who volunteered, took part with no drop-outs. For the age-matched control cohort, the only inclusion criteria were that participants should also be aged over 55, and the exclusion criteria was that participants should have a healthy retina.

5.1 Introduction

Age-related macular degeneration (AMD) can result in loss of central vision, and is the leading cause of visual impairment in adults (> 50 years) in the UK [5]. In 2012, the prevalence of AMD was predicted to increase significantly by 2020 due to aging of the population [15, 16].

The Age-Related Eye Disease Study (AREDS) [12] reported that taking a supplement containing vitamins E and C, beta-carotene and zinc reduced risk of progression of the disease by 25%. Since then, the carotenoids lutein (L), zeaxanthin (Z) have been identified as nutrients that can provide a protective role in the progression of AMD due to their antioxidant and photo protective properties [168]. Collectively, L and Z form the macular pigment which interacts with free radicals and reactive oxygen species, prevent lipid peroxidation and filter out high energy blue light [147]. Carotenoids are not produced by the body and must be obtained via the diet. Recently, the AREDS II [150] found that people who took a supplement containing L and Z instead of beta-carotene had their risk of progression reduced by a further 18% compared with the original AREDS formulation [150].

Despite results from AREDS studies, there remains confusion among patients and practitioners in what supplements to take, and what foods should be consumed in order to maximise absorption of useful nutrients [105]. Many patients turn to other organisations for clarity of information such as the Macular Society – the UK charity that is devoted to helping those with diseases of the macula. Following the results of AREDS II, the Macular Society have advocated the use of the AREDS II formulation, where appropriate, and eating vegetables that are L&Z rich. The highest mole percentage of L&Z has been found to be in egg yolk, maize (corn), spinach, collard greens and kale [151].

Patients who have sought the help of the Macular Society could be considered an 'informed' population as they have information available to them in the form of monthly magazines, written material, a helpline and the Society's website. However, in a recent study, not all were taking a nutritional supplement and many of those that did take a supplement were not taking a clinically proven formulation or dosage [140]. We therefore sought to investigate this population's dietary intake of L and Z, and compare it to a cohort of age matched patients without the condition. As dietary patterns are multi-factorial, any other contributing factors will be investigated.

The objectives of this study were to analyse the nutrient intake of a group of AMD patients and a group of non-AMD patients, and to determine their ability to prepare and cook healthy food.

5.2 Materials and Methods

Using data from a previous study by Bartlett et al, it was calculated that for an average effect size (Cohen's d) of 0.4, a minimum sample size of between 15 and 94 would be appropriate for each cohort [74].

AMD Participants

A total of 158 participants with AMD were recruited between January 2012 and March 2012. Recruitment was via the Macular Society helpline. Individuals who contacted the Macular Society helpline between January 2012 and March 2012 were asked if they would like to take part in a telephone survey. Inclusion criteria for potential participants were that they should be aged over 55 years and have been diagnosed with any form of AMD.

Non-AMD Participants

A group of 50 participants without AMD were recruited between August 2013 and December 2013. Recruitment was via seven optometric practices around the UK and Aston University patient clinics. The study was advertised on posters, and individuals who took part volunteered of their own accord and provided contact details and a convenient time to be telephoned. The only inclusion criterion was that they should be aged over 55 years – individuals with co-morbidities and other visual problems were not excluded.

Survey Design

A 36 question cross-sectional survey was designed to explore nutritional habits, supplement usage, physical abilities in food preparation and cooking, and sources of knowledge in order to ascertain the beliefs participants have, and compare their beliefs with their behaviours. The initial questions covered demographic topics, occupations and participants' perceptions of the link between nutrition and AMD. The terms 'wet' and 'dry were employed to coincide with many patient's understanding of AMD classifications. After a section on nutritional supplement use, the questions subsequently focused on perceived state of vision and health, and ability to perform preparation and cooking of food. Participants also provided a 24 hour food recall. This was done as part of the telephone survey so the patient had little time to prepare and would be more likely to report honestly. Participants were asked to quantify the amounts of food eaten by using the Zimbabwe Hand method [169] – participants used their palms or fingers to estimate the portion size of various foods. The survey was then piloted, refined and administered to the cohort. Full details of the piloting process and survey design and are reported in **Chapters Three and Four** [140]. The focus of this report is on the dietary aspects of this survey and cooking abilities, hence, not all the results of the 36 questions are covered here (10). The participants' occupations were divided into 10 major groups using the International Standard Classification of Occupations (ISCO) version 08.

The 24 hour food diary data was analysed using nutritional software A La Calc (Red Hot Rails LLP, Doncaster, UK.), where each participant's daily food was analysed for numerous nutrients, calorie values and other constituents using the USDA (United States Department of Agriculture) SR25 food database (http://ndb.nal.usda.gov/).

Procedure

If an AMD patient decided to participate, oral informed consent was obtained over the telephone and they were advised that they could withdraw at any time. An appointment was scheduled for a future telephone interview or the interview began immediately if the AMD

patient agreed. Non-AMD patients who provided their contact details were telephoned at a time that they specified was convenient, and the interview usually began immediately. The survey typically lasted 25 minutes and was administered either by one of four Macular Society employees who were trained by RS or by RS. All responses were recorded using Bristol Online Survey software (University of Bristol, Bristol, UK) [140].

Data and Statistical Analysis

Descriptive analyses were performed using the software Microsoft Excel. Data was then analysed in statistical software IBM SPSS version 20 (IBM UK Ltd, Portsmouth, Hampshire) to draw comparisons between results using parametric and non-parametric tests as not all the data was normally distributed.

Ethics

This study was conducted according to the guidelines laid in the Declaration of Helsinki and all procedures involving human subjects were approved by the Aston University Ethics Committee. Verbal informed consent was obtained from all subjects and formally recorded.

5.3 Results

Sample Characteristics: AMD Participants

Table 4.1 shows some of the demographic characteristics of the sample; AMD participants were aged 56-95 (mean 79 ± sd 7.8 years). Of the AMD cohort, 61% were female, with both genders showing similar age distributions. The prevalence of 'wet' and 'dry' types of AMD was almost equal. The mean duration of the disease was 6.08 ± 4.7 years (median 5 years, range 1 to 25 years). The majority of AMD participants (63%) were not registered sight impaired (partially sighted) or severely sight impaired (blind). There was a trend for participants who were on a visual impairment register to have had AMD for a longer time period (Mann-Whitney $U = 977.5$, $p = 0.07$). No AMD participant felt that their vision was "extremely good" on the day of the interview - 57% of participants felt their vision was "poor" or "extremely poor" and only

7% felt their vision was “good”. These results contrast with perceptions of general health in that only 21% of AMD participants felt their general health was poor, and 41% felt their health was good. For these reasons, the sample was considered to be a healthy population whose only health issue was their visual status.

Sample Characteristics: Non-AMD Participants

Non-AMD participants were aged 55-89 (mean 67 ± 8.0 years). Of the non-AMD group, 70% were female, with both genders also showing similar age distributions. On the day of the interview, the majority of the non-AMD participants felt their vision was either “extremely good” (14%), or “good” (46%). No participant felt their vision was “extremely poor”. 70% of the non-AMD participants reported they felt their general health was either “good” or “extremely good”. This cohort can also be considered a healthy population

The cohorts have some similarities in the reported characteristics. A high percentage of participants in both cohorts lived in their own home, and only a few lived in sheltered accommodation. However, half of the AMD participants lived with their partner, with just under half living alone, but in comparison, fewer of the participants without AMD lived alone and more lived with their partner. Also, more participants in the AMD cohort answered that they felt their general health was ‘poor’ compared to the participants without AMD. Unsurprisingly, the largest difference between the cohorts was the self-reported visual ability, with many of the AMD cohort reporting ‘poor’ vision.

Because the non-AMD participants were generally younger than the AMD group (mean 67 years, versus 79 years), a sub-group of age-matched AMD participants (49 participants in total) were used to compare data with the non-AMD cohort.

Characteristic	Characteristic	Percentage of AMD participants	Percentage of non-AMD participants
Living Arrangements	Own home	88%	96%
	With family/friends	3%	0
	Sheltered accommodation	7%	4%
	Other	2%	0
With	Partner	50%	66%
	Alone	46%	30%
	Other family members	4%	4%
Registration	Blind	16%	Not applicable
	Partially sighted	21%	Not applicable
	None	63%	Not applicable
General Health	Extremely good	7%	22%
	Good	41%	48%
	Satisfactory	19%	20%
	Poor	21%	8%
	Extremely poor	3%	2%
Vision	Extremely good	1%	14%
	Good	7%	46%
	Satisfactory	35%	32%
	Poor	42%	8%
	Extremely poor	15%	0

Table 4.1 Selected demographic characteristics of both AMD and non-AMD participants.

Dietary Analysis

Table 4.2 displays the results of the 24 hour food diary data for the AMD and non-AMD participants. The mean amounts of certain nutrients or energy consumed for females and males in the cohort are displayed, together with the recommended dietary allowances (RDA)

for each constituent, as recommended mainly by the UK Food Standards Agency (FSA) for those aged over 50 years. **Table 4.2** shows that in the AMD cohort, both men and women fail to meet the daily RDA for many nutrients such as fibre, calcium, vitamin E, folic acid and carbohydrates. Of particular interest is the finding that in the AMD cohort, both genders are failing to reach the 10mg amount of daily L&Z recommended by the Macular Society. Although not statistically significant, there was a trend that those who were on a sight impairment register consumed more L&Z than those AMD participants who were not on any type of register (Kruskal Wallis H = 4.951, p=0.08), and females appeared to consume more L&Z than males in the AMD group. One male participant's diet data was excluded as he had unusually consumed a large amount of kale, and the results were slightly skewed (the average with this participant included is listed in the table in parenthesis). L&Z consumption was compared with the type of AMD the participants had (dry vs. wet), occupation, and the number of years they had the condition, but no trends were apparent. The amount of L&Z was also low in both genders of the non-AMD group.

The largest difference between the two cohorts was the number of calories consumed. The number of calories consumed by the AMD cohort was significantly lower than the daily RDA for each gender in this age group. This difference in calorie intake between the AMD and non-AMD cohorts is statistically significant (independent t-test F= 19.2, p = 0.00). In contrast, females in the non-AMD cohort surpassed the calorific RDA, and males in the non-AMD cohort also consumed nearer to the RDA. Other nutrient differences between the cohorts included carbohydrates, protein, fat, fibre and calcium - participants with AMD consumed less compared to participants without AMD, but not with statistical significance.

There were no significant gender differences found with respect to the amount of L&Z consumed, the number of calories consumed, the ability to cook a hot meal or supplement use in either cohort (Kruskal-Wallis and Mann-Whitney U non-parametric tests). Calorie intake was also compared with the age of participants and living arrangements in each cohort, but no significant results were found. Employment between the two groups were also analysed, but the differences between them were not found to be statistically significant (Independent t-test).

		AMD Female (Mean) (n = 96)	AMD Male (Mean) (n = 62)	Non-AMD Female (Mean) (n = 35)	Non-AMD Male (Mean) (n = 15)	Females RDA >50 yrs	Males RDA >50 yrs
Energy	Kcal	1524	1507	2251	2074	1800	2200
Energy	kJ	6375	6076	9417	8674	7200	8700
Lutein and Zeaxanthin	Mg	1.7	1.2	1.6	1.3	10	10
Protein	G	61.8	64.1	94.5	82.0	45	55
Fat	G	65.4	60.5	86.8	82.3	70	95
of which saturates	G	27.7	25.4	30.8	30.6	20	30
Carbohydrates	G	177.2	169.0	278.6	257.5	230	300
of which sugars	G	50.5	44.7	90.9	61.8	90	120
Fibre	G	16.7	16.1	24.6	22.4	24	24
Cholesterol	Mg	252.9	300.8	354.6	408.0	300	300
Calcium	Mg	682.9	644.0	948.0	980.5	800	800
Iron	Mg	14.5	16.1	22.4	20.4	10	10
Retinol	mg	0.4	0.4	0.4	0.6		
Carotene	mg	0.4	0.7	0	0		
Alpha Carotene	mg	1.1	1.4	1.1	1.3		
Beta Carotene	mg	3.5	4.1	3.8	4.0		
Vitamin D	µg	2.6	13.5	2.4	3.5	5	5
Vitamin E	Mg	5.0	5.1	7.6	6.0	10	10
Vitamin C	Mg	53.1	62.1	85.6	82.3	40	40
Folic Acid	µg	167.8	252.2	214.4	185.7	400	400

Table 4.2. Mean consumption of various nutrients for males and females in both the AMD cohort and the non-AMD cohort, with the corresponding RDA for people aged over 50 years. Kcal refers to Kilocalories, kJ Refers to Kilojoules, Mg refers to milligrams, µg refers to micrograms and G refers to grams. Spaces indicate there are no RDAs for that nutrient.

Many participants in both cohorts ate only a small variety of vegetables: 140 participants listed carrots, 116 listed peas, 115 listed broccoli. Other popular choices were cabbage (90 participants) and spinach (49 participants). Interestingly only 25 AMD participants ate kale which is considered to be one of the most lutein rich vegetables. No participant in the non-AMD cohort ate kale at all. Interestingly, 85% of AMD participants ate mostly raw vegetables on the day of the interview, but 62% of non-AMD participants ate cooked vegetables on the day of the

interview. On the interview day, 10% of the AMD participants and 8% of the non-AMD participants did not eat any vegetables at all.

Food preparation and cooking

The majority of participants reported they could prepare (65% AMD, 74% non-AMD) and cook (68% AMD, 72% non-AMD) their own food, with participants citing that their partner prepared (24% in both cohorts)/ cooked (26% in both cohorts) food for them. When asked if participants were able to cook a hot meal by themselves if they had to, 81% of AMD and 96% of non-AMD participants reported that they could. Participants with AMD who were not able to cook a hot meal (n=29) consumed significantly less L&Z (0.85 ± 0.72 mg) than those who were able to cook a hot meal (1.68 ± 2.35 mg) (Mann-Whitney U = 1240.5, p = 0.007). **Figure 4.1** shows that many AMD participants feel that they are able to cook and prepare food and that there are no barriers to changing their diets other than that they do not wish to.

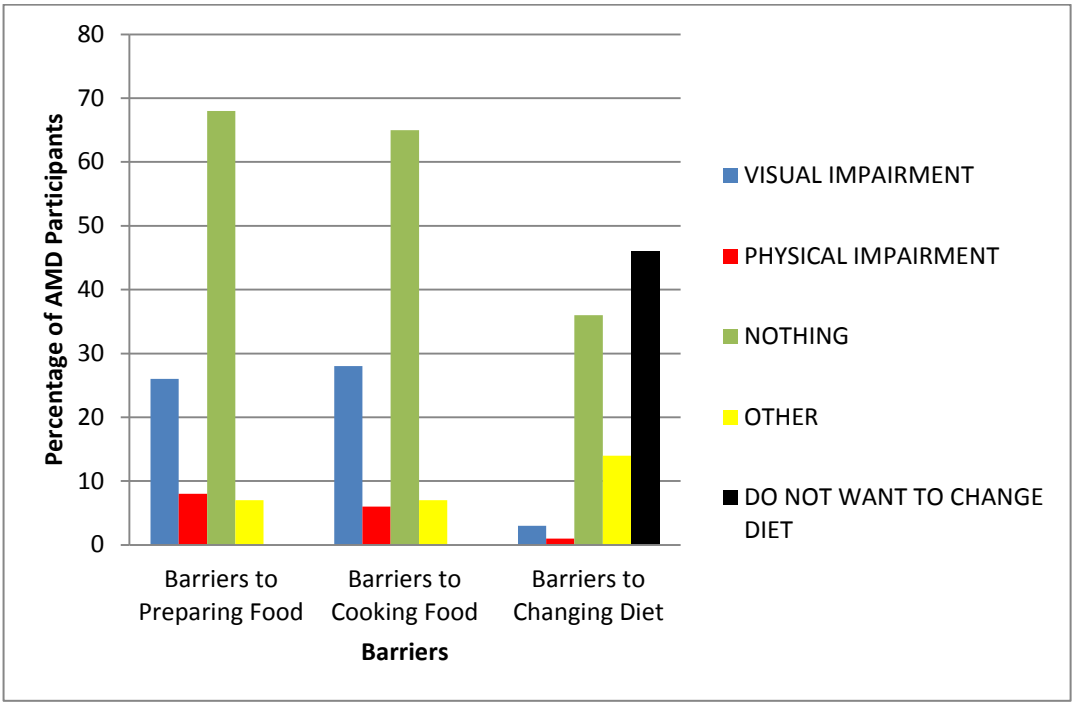


Figure 4.1. AMD participants perceived barriers to cooking food, preparing food and changing diet.

Fifty six percent of AMD and 86% non-AMD participants were self-sufficient in carrying out their own food shopping; whilst for 28% of AMD respondents and 14% of non-AMD respondents, a family member did this task for them. Less AMD participants were therefore self-sufficient than non-AMD participants, and this will impact on food choices and food consumption. The remainder of the respondents used other methods to obtain their food needs such as Meals-On-Wheels (Social Services) or friends. Participants were asked to identify all of the sources from which they acquire food. Supermarkets were reported by 135 participants, and 36 also reported they purchased food from a local shop. Some 12 participants harvest their own food. Only four AMD participants relied upon delivered ready meals such as Meals-On-Wheels. The main reason for selecting the type of food appears to be preference (44% AMD, 46% non-AMD), secondary to the effect on health (34% both cohorts). Only 4% of the AMD group, and 8% of the non-AMD group listed 'habit' as an influencing factor.

Age-matched comparisons between AMD and non-AMD participants

Because the AMD participants were older than the non-AMD participants, it was appropriate to compare the non-AMD group with an age-matched sub-group of AMD participants (n=49). The mean age of the sub-group was 68.8 years, and this did not differ significantly from the AMD group (Spearman 0.063, p=0.662). Eighty-six percent of the group were female. There were a higher percentage of participants in the sub-group that felt that their health was 'extremely good' (16%) and this is close to the percentage of non-AMD participants (22%).

Table 4 shows the mean diet results of the aged-matched sub-group of AMD participants, with the overall mean diet results from the non-AMD cohort alongside. In this comparison, the difference between the AMD participants and the non-AMD participants is still significant; the non-AMD group consumed more of each nutrient analysed than the AMD age-matched sub-group. The average energy intake for AMD participants was 1502 kilocalories compared to 2198 kilocalories consumed by non-AMD participants (paired t-test $p<0.001$). However, the exception to this rule was the L&Z intake, where the average consumption was not statistically significantly different (1.8 mg in the AMD group versus 1.5 mg in the non-AMD group, $p= 0.97$).

	AMD Sub-Group Mean (n=49)	Non-AMD Mean (n=50)
Age (years)	68.8	67.5
Energy (Kcal)	1503	2198
L&Z (mg)	1.8	1.5
Protein (G)	60.9	90.8
Fat (G)	61.9	85.5
Carbohydrates (G)	166.9	272.3
Fibre (G)	15.6	24
Vitamin E (mg)	5.3	7.1
Beta Carotene (µg)	3.2	3.9
Vitamin C (mg)	56.9	84.6
Folic Acid (mg)	0.2	0.21
Calcium (mg)	596.1	887.8

Table 4. Mean age and energy/ nutrient consumption for the selected AMD subgroup and the non-AMD group. Please note: Kcal refers to Kilocalories, kJ Refers to Kilojoules, µg refers to micrograms, Mg refers to miligrams, and G refers to grams.

5.4 Discussion

This sample of people with AMD consumed an average of 1.4 mg of L&Z per day. This is below the 10mg daily amount considered to be required for augmentation of macular pigment [85]. In addition, they were not attaining the RDA of other nutrients such as vitamin E and calcium. Those that were not able to cook a hot meal by themselves consumed significantly less L&Z than those that were able to cook a hot meal. Participants were not consuming enough calories for their age group, and were adhering to a diet with little variety. Many participants were not consuming the L&Z-rich vegetables, such as spinach and kale. A sample of non-AMD patients consumed calories and other nutrients much nearer to the RDA, and consumed an average of 1.5 mg of L&Z.

In terms of differences and similarities between the AMD participants and the non-AMD participants, the demographic characteristics were similar. Both groups ate a limited variety of foods, and consumed similar amounts of L&Z, indicating that AMD participants were not

consuming much more than those without the condition. However, the amount of nutrients and energy consumed was quite different between the groups, as the non-AMD cohort consumed much more than the AMD group and in some cases even more than the RDA.

The majority of AMD participants felt their vision was poor on the day of the interview. However, this visual impairment did not impact on their kitchen abilities as most participants felt able to cook a hot meal, go shopping and obtain food from a supermarket themselves. Many felt that their vision or physical capability was not preventing them from changing their diet should they wish to; many did not want to change their diet. The main factor that influenced participants' food choices was preference, indicating that participants would only eat food if they liked it.

Since the AMD cohort all had a form of AMD, and were motivated to contact the Macular Society for assistance, it has been assumed that they were interested in preventing the disease from progressing. All would have received diet advice from the Macular Society, if not from their ophthalmologist. Overall, however, participants were not consuming enough of the majority of the nutrients recommended, particularly L&Z. The reasons behind this are likely to be multi-factorial – dislike for the nutrient-rich foods, lack of knowledge of how to cook or prepare them, misjudging the amount required per day, or lack of control (family or caregivers cook food). The most likely reason is because dietary habits are difficult to change - especially with increased age [170]. L&Z intake was associated with those who were able to cook a hot meal, indicating that those who were more proficient in the kitchen were able to consume these foods more easily.

There does not seem to be evidence that information received from the Macular Society or other sources modified participants' behaviour. Ley's model on effective communication in medical practice [171] stresses the importance of memory next to factors such as the understanding of information and satisfaction with the treatment. Indeed, 40–80% of medical information provided by healthcare practitioners is forgotten immediately [172]. The greater the amount of information presented, the lower the proportion correctly recalled [173], furthermore, almost half of the information that is remembered is incorrect . Studies have proposed three explanations for memory loss—first, practitioner factors, such as use of medical jargon; second, the type of information (e.g. verbal, written); and, third, patient factors, such as low education or specific expectations [172].

With respect to medical information, an inverse relationship has been reported between age and amount of information correctly recalled [172]. However, although older adults have difficulty spontaneously recalling medical information, they are able to take advantage of cues to access verbally learned information [174]. Studies into patient compliance have shown that patients rarely adhere fully to practitioner advice [175], and AMD patients are reported to have not complied with recommended dietary supplement advice [118, 140].

Patients often report that they do not receive any advice from their ophthalmologist or optometrist regarding nutrition [140]. This may be partly due to the profession's differing opinions on nutrition research REF, but a patient's recall difficulties when given medical advice may also play a role.

Other nutrients and energy

With the exception of iron and protein, AMD participants did not meet the RDA of the nutrients analysed. AMD participants' energy intake was lower than recommended for their age-group and gender. This lowering of energy intake with increasing age has been found in other studies and some suggest that this is a physiological response that older adults exhibit in reaction to a decline in physical activity [176]. Some studies [177, 178], suggest that those living alone might consume fewer calories than those living with others, although we found no such relationship. A study into eating habits of older adults found that they eat more when they are presented with variety, and this variety is the key to increasing calorific consumption [179]. However, the non-AMD cohort managed to reach the RDA of many of the nutrients analysed, including calories. It may be argued that this was because there were fewer participants in the sample, and the average age of the sample was younger. However, when an age-matched cohort was analysed, the same differences in dietary intake was found. The non-AMD cohort did not eat a more varied diet either; they appeared to just eat more food than the AMD group. The cause of this is likely to also be multi-factoral; it has been shown in studies that poorer vision impacts on an individual's appetite [180, 181]. More AMD participants were reliant on other people to shop and prepare and cook food, and this also may limit the amount they eat.

The Hertfordshire cohort study [182] found that two patterns of diet are prevalent in the older adult group – a 'prudent' pattern that is characterised by fish, fruit, vegetables and wholemeal cereals, and a 'traditional' pattern characterised by vegetables, processed meat and puddings. The comparison between occupation and nutrients did not show any statistical trends in our results, but it was noted that 62% of AMD participants and 76% of non-AMD participants adhered to a 'traditional' pattern of eating with limited choices of vegetables and fruits, and

traditional British recipes such as pies, stews and roast meats. This conservative variety of vegetables saw only a minority of AMD participants consuming the lutein-rich kale on a weekly basis, although more participants did eat spinach.

Strengths and weaknesses

This sample may not represent all AMD patients seeking services from organisations like the Macular Society. It is also important to find out the opinions of those with AMD who have not sought support from non-professional organisations. The sample sizes are different, and have been discussed. A more detailed food recall might have enhanced the study, especially to view eating patterns. This could be performed over a number of days rather than 24 hours. It would have been beneficial to gather other data such as participant's BMI and activity levels to compare to calorific intake. It is conceivable that a difference in BMI between the groups might have accounted for some of the dietary differences reported, but as this data was not collected, it is impossible to determine this. The investigators feel that it is unlikely that differences between the groups are due to differences in BMI alone, as a previous study reported lower calorie intake in visually impaired participants [74] and other studies show that food intake and dietary patterns do not appear to differ with various BMIs [183-185]

Results show that participants were not in poor health generally, suggesting that results relate to issues with visual impairment only. Practitioners need to be consistent and unified in the advice that is given to patients, if confusion is to be avoided. The results also show that, in spite of advice being given to patients, they primarily eat food they enjoy and are used to. Changing eating habits therefore, requires novel intervention methods. It is essential to design effective measures for imparting and disseminating appropriate dietary and supplementation advice for patients with, or at risk of, AMD. The following chapter will introduce and discuss one intervention design to impart appropriate dietary and supplementation advice for patients – a clinical decision making aid.

Chapter Six

Development of a Clinical Decision Making Aid

Chapters four and five presented the results of the cross-sectional survey administered to participants with and without AMD. The results showed that participants with AMD did not feel that they had enough information on nutrition and when questioned about particular fruits and vegetables, many did not know which would be beneficial for eye health. A twenty-four hour food diary showed that participants with AMD were not eating enough of these helpful nutrients, and were not eating enough food overall when compared to participants without AMD.

In order to make a difference in AMD patient's lives, a practitioner based intervention is required. Many of the participants expressed a lack of information from their eye-care practitioners, and research has shown that the professional opinions are divided in this area [164]. There are no clear-cut guidelines currently for patient or practitioner to follow [166], and the latest study AREDS 2 has provided clarity due to the complexity of the study. The logical start to an intervention would be to tackle practitioners first to ensure that the correct information is being passed on to patients in the first instance. This chapter discusses the background and methods employed for the intervention: a clinical decision-making aid.

6.1 Background

When presented with a patient, all clinicians ultimately must answer three questions [186]:

1. What disease/ condition does this patient have?
2. Should this patient be treated?
3. Should testing be done?

These three questions are often riddled with uncertainties, and decisions must be made to avoid wasting time. Decision making; a "choosing of alternatives" [187] in medicine is varied and can range from intuitive decisions through to well-reasoned, analytical, evidence-based decisions that drive patient care [188]. Practitioners of medicine and allied health will often use their experience and intuition to informally decide clinical care in simple, common conditions. Decisions will often be made based on existing practice. However, where complex decisions with a high level of uncertainty need to be made, practitioners will often use a more methodical

approach in order to feel supported [188], such as clinical guidelines, quantitative techniques and evidenced-based principles.

Evidenced-based medicine / practice can be defined as integrating the judicious use of current best evidence in clinical decision making, together with patient values and clinical expertise[189]. A series of steps can be used to formulate a strategy for an individual patient. These steps include articulating a clinical question, gathering evidence to answer the question, evaluating the quality and validity of the evidence, and finally deciding how to apply the evidence to the care of a given patient [190]. The rationale is that this type of decision making mitigates the use of unnecessary resources. However, these steps can be time consuming, and as the pressures of current health systems continue to increase, it is often reserved for only the very complex clinical cases [190]. A case study used by Courtney *et al*., is of a high-risk intensive care patient with a short-term intravascular catheter [191]. The decision to be made is whether to change the catheter administration set at regular intervals or not – changing the sets is costly and obviously involves practitioner time. Many practitioners have historically changed administration sets regularly as they believed it reduced the risk of contracting a nosocomial infection secondary to the use of an intravascular catheter. When reviewing the evidence available, several studies show that infection levels did not differ when the sets were changed at different time intervals. One study however, was a randomised controlled trial (a good quality study) which showed that the expensive and time-consuming procedure was not effective in high-risk intensive care patients with short term catheter use. The decision here becomes obvious – for this particular patient, the administration sets do not need to be changed at regular intervals.

Models

Clinical decision making models in medicine have been described for many years, particularly for front-line doctors and nursing staff. Nursing researchers Banning *et al* proposed that there are three main types of models [192]:

Information- processing model

This model uses a scientific or hypothetical / deductive approach to assist metacognitive reasoning that is essential to medical diagnosis[193]. Decision 'trees' are used to assess potential outcomes by assigning a number to each potential outcome and a probability of attaining an outcome is given. For example, **Figure 5.1** shows a decision tree of using a particular medication for the treatment of ulcerative rectocholitis.

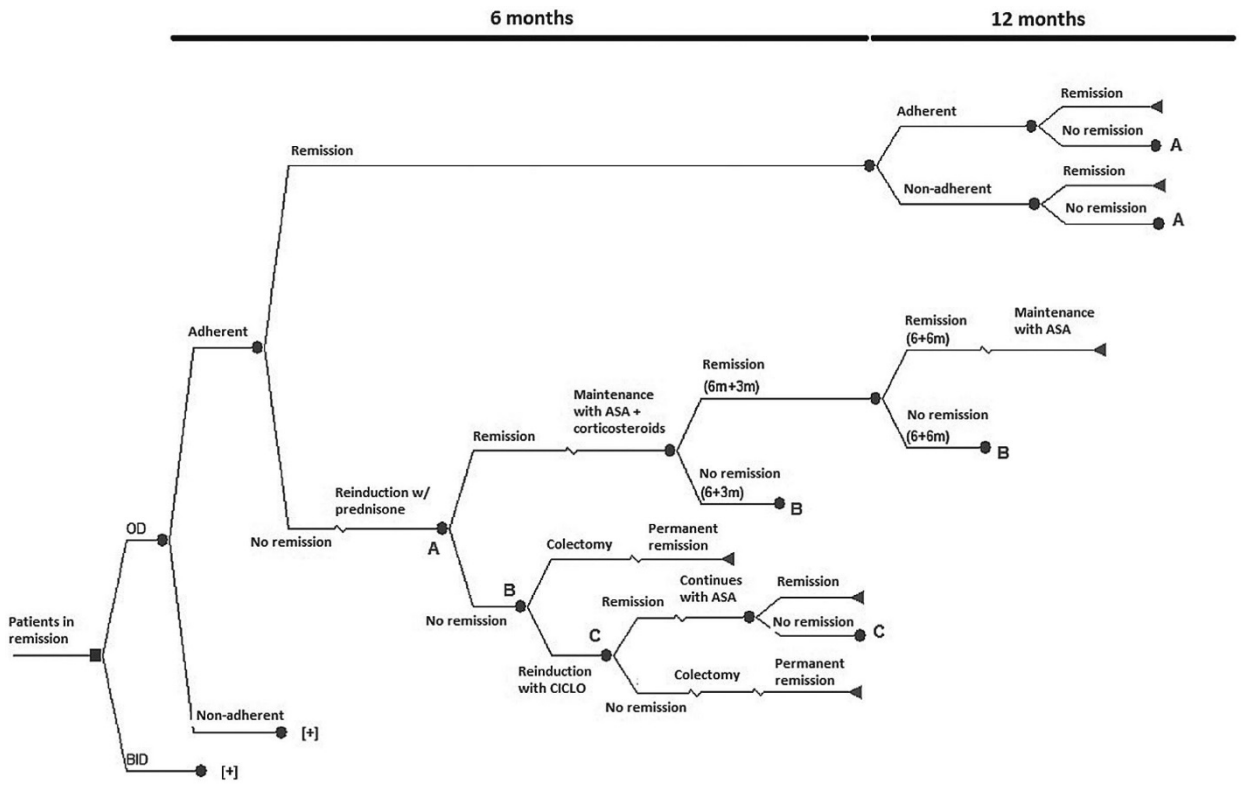


Figure 5.1 Decision tree depicting patients in remission of unspecified ulcerative rectocolitis given the option of treatment with a drug (Pentasa) under two dosing schedules (o.d. or b.i.d). **Table ??** below shows the probability of remaining in remission in both doses tested.

	Probability of maintaining in remission	
Time	**Adherent**	**Non-adherent**
6 months	100% (90%-100%)	60% (54%-60%)
12 months	84% (76%-92%)	59% (53%-65%)

Intuitive- humanist model

Rather than relying on guidelines, procedure and scientific reasoning, practitioners use their experience and intuition to make clinical decisions. For example, many optometrists use their intuition when recommending certain optical appliances such as contact lenses based on previous experience of how the appliances fit, move and are used by various patients.

O'Neills multidimensional model

This theoretical model is based on a computerised decision support system that uses both hypothesis and pattern recognition for use by inexperienced nurses. This model contains five

elements including pre-encounter data, anticipating and controlling risk, the provision of standard nursing care, client and situational modifications, and finally hypothesis generation and testing. This model cuts loose the inflexibility of guidelines by accounting for the many variables that exist in life, and inexperienced practitioners can easily input in the data to generate an answer.

Figure 5.2 shows how all the different aspects of decision making overlap, and need to, in order to decide which the best solution is for a patient.

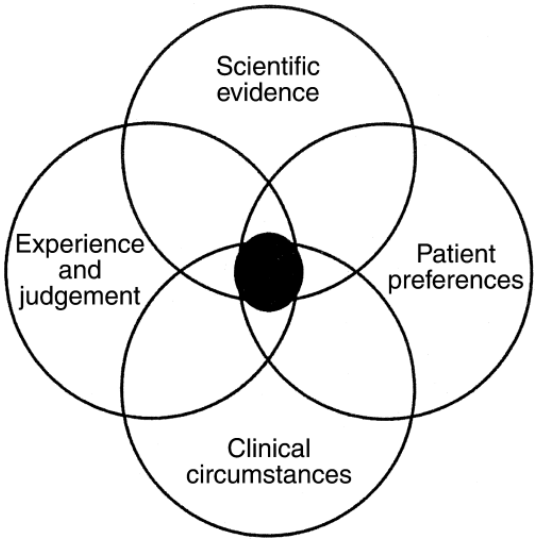


Figure 5.2 Intersection diagram of clinical decision-making process [194, 195].

Clinical guidelines have been created by many speciality societies (e.g. NICE or WHO) using the principles of evidence based medicine and also the consensus of a panel of experts. Patients are often put into a category or group, and the guideline will follow a 'if, then' rule with a number of multi-steps if the question is particularly complex [190]. These guidelines are often inflexible and it can be difficult to place some patients into specific categories, but, for a busy overstretched clinical practice, they can be invaluable. Sometimes these guidelines are depicted using decision-making aids such as decision trees, flow charts, and brainstorm and mind map diagrams. **Figure 5.3** shows such an example of a NICE 'pathway' – many other medical conditions are indexed in the NICE pathway website for practitioners to download.

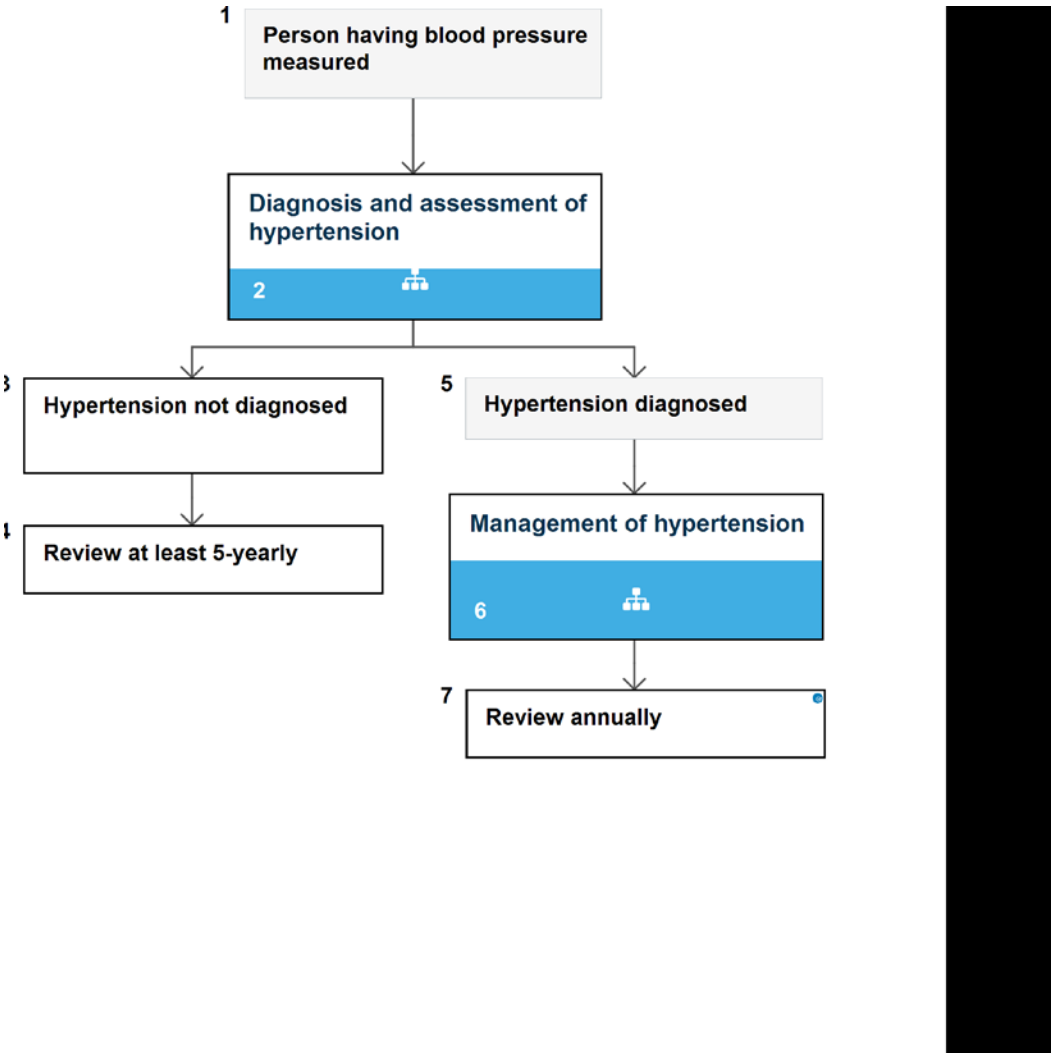


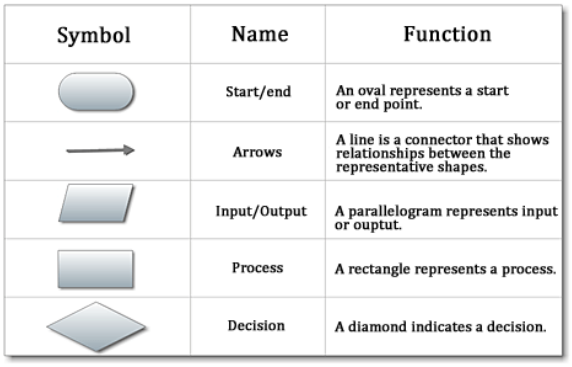
Figure 5.3 NICE pathway for clinical management of primary hypertension in adults. The numbers indicate the various steps.

Decision flow diagrams

As shown in **Figures 5.1** and **5.3**, decision 'trees', flow diagrams, information flow diagrams, pathways or flowcharts are tools that show the visual representation of the sequence of steps and decisions needed to perform a process linked together by connecting lines and directional arrows. They have been historically used by industrial work engineers to structure work but now they are used in medicine and many other disciplines[196]. They can be used as a 'plan map' to pictorially describe the various stages of a project, or to describe a process. They can be used an efficient alternative to written documentation. They can also be used to brainstorm computer algorithms, and to help aid decision making. Many flowcharts used in eye care

consist of either differential diagnosis or treatment decisions - please see **Appendix 8** for an example of a flowchart used in optometry [197]

Different flowcharts have evolved over time – swim lane, data flow, influence, work flow, process flow and many more. The design of a flowchart is important – the start and end points must be decided before hand, with the most efficient path of getting between them, and the flow of the diagram must either run horizontally or vertically. The start and end points are depicted with shapes that have rounded edges, the decision points are depicted as diamonds. Above all, flowcharts must be simple enough for anyone to understand.



Symbol	Name	Function
	Start/end	An oval represents a start or end point.
	Arrows	A line is a connector that shows relationships between the representative shapes.
	Input/Output	A parallelogram represents input or ouptut.
	Process	A rectangle represents a process.
	Decision	A diamond indicates a decision.

Figure 5.4 Symbols of flow charts [196].

As stated, flowcharts have been used in medicine to aid diagnosis, treatment options and advice given to patients. Because they use symbols or diagrams, they are able to be used in high pressured environments where time is limited, since users can absorb information very quickly. Flowcharts are often space efficient too, and can be placed on surgery walls or pin boards so practitioners can have easy access. As such, a flowchart would be an ideal clinical decision-making aid for all practitioners to use, and an ideal way to implement an intervention for better nutritional advice for patients with AMD.

6.2 Objectives

The aim of this intervention was to design a flowchart that can be used to decide what advice to give to patients seen in optometric and ophthalmic practices, universities or hospitals, by all eye-care practitioners with ease. Outcomes of the intervention should include increased practitioner knowledge and less inter-practitioner variability when giving patient advice.

5.3 Clinical decision-making aid design

As mentioned, modern medical practice has used flowcharts and diagrams to aid diagnosis and decision making [196]. For an aid to be successful, it needs:

1. To answer a particular question (or questions)
2. To be small enough in size to fit in a folder or be on a wall without taking too much physical space
3. To be succinct enough to fit the important information in one place
4. To have distinct clinical processes with final outcomes or decisions

For this intervention, a flowchart design is the most appropriate. The decision or question that needs to be answered in the flowchart is: “when and what nutritional advice to give to patients with, or at risk of, AMD”. The only large scale clinical research that is currently available to answer this question is the AREDS 2 study; the study’s participants’ inclusion and exclusion criteria can be used to decide when it is appropriate to advise the AREDS 2 supplementation (the only supplement preparation that is appropriate to advise at this point in time).

AREDS 2 inclusion and exclusion criteria

The AREDS 2 participants were divided into four primary groups: those that received L&Z only, those that received L&Z plus omega 3 fatty acids, those that received omega 3 fatty acids only, and those that received a placebo. The four primary groups were further divided as shown in **Figure 5.5**.

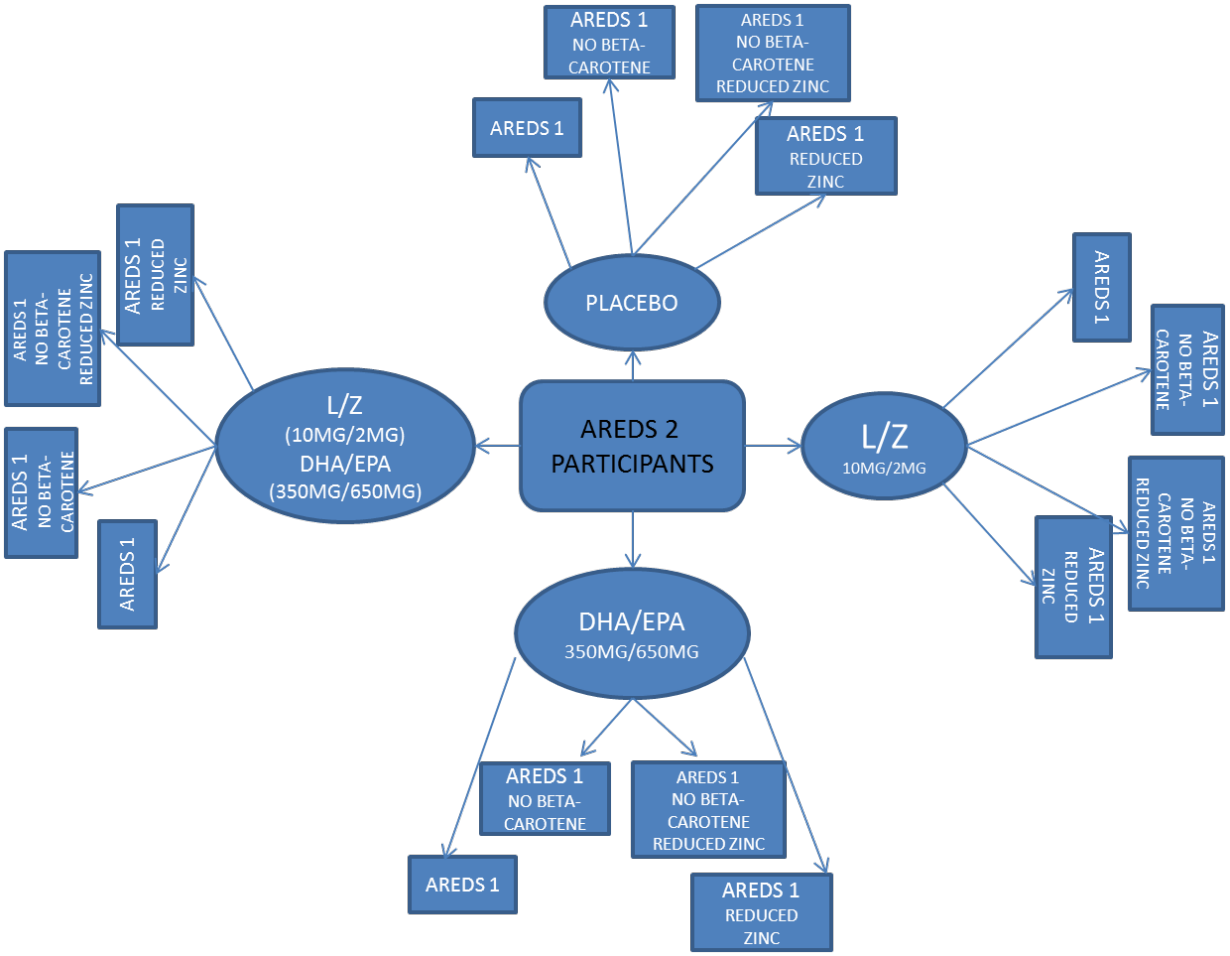


Figure 5.5. The groupings of participants in the AREDS 2 study.

Participants were either men or women aged 50 to 85 years at the qualification (initial) visit. They had to have bilateral large drusen (≥ 125 microns) or large drusen in one eye and advanced AMD in the fellow eye. A study eye (eye without advanced AMD) may have had definite geographic atrophy not involving the centre of the macula without evidence of drusen.

Based on these inclusion criteria, if a patient is over 50 years old, has bilateral large drusen or drusen in one and advanced AMD/ definite geographic atrophy in the fellow eye, it can be said that they could benefit from the AREDS 2 formulation. (The study encompassed L&Z (carotenoids) to the original AREDS supplement formulation, and the study results show that substituting L&Z for beta-carotene reduced risk of progression by an additional 18% on top of the original 25% risk reduction found in AREDS 1 – see section 1.7).

Construction

The flowchart was initially drafted in Microsoft Word using the shapes function, as seen in **Figure 5.6**. The top of the flowchart started with the findings on ophthalmoscopy – as unusual macula appearance. If a patient had a normal macula, but had a family history of AMD, a branch of decisions was created to determine whether they would benefit from dietary modification. If the patient did have a non-normal macula, the branches following determined whether the patient fitted into the AREDS 2 inclusion criteria, or whether they would benefit from dietary modification only. If the findings were not related to AMD, referral for an ophthalmological opinion was advised. The final outcomes were split into either dietary modification (advice one), or supplementation (advice two).

Once the design had been decided upon, the chart was then created in flowchart software Lucidchart (Lucid Software Inc., 282 East 12000 South Suite 200, Draper, UT 84020, US), with 'yes' and 'no' decision lines, as seen in **Figure 5.7**. (A full size copy is in **Appendix 9**)

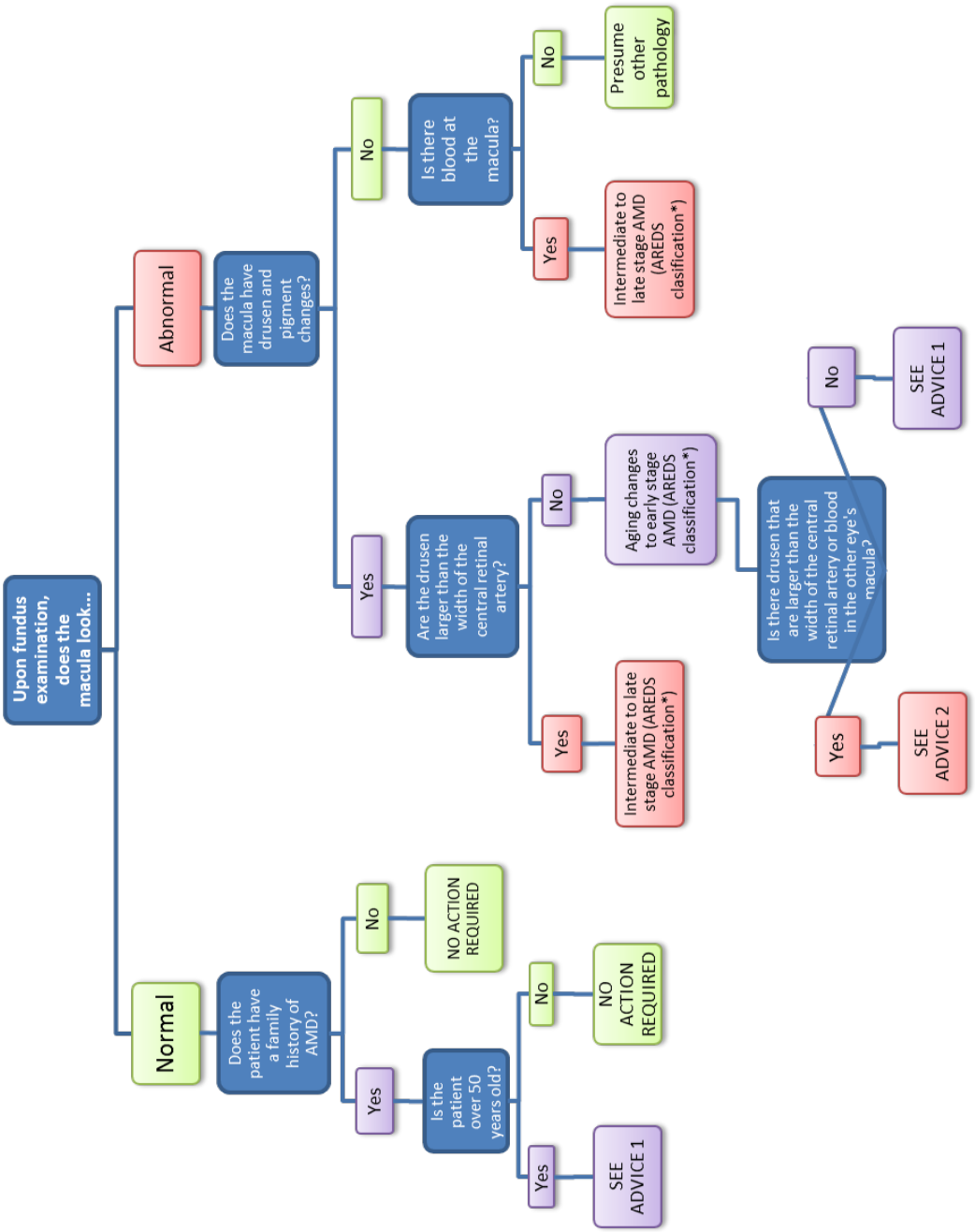


Figure 5.6 Initial design of the flow chart using Microsoft Word.

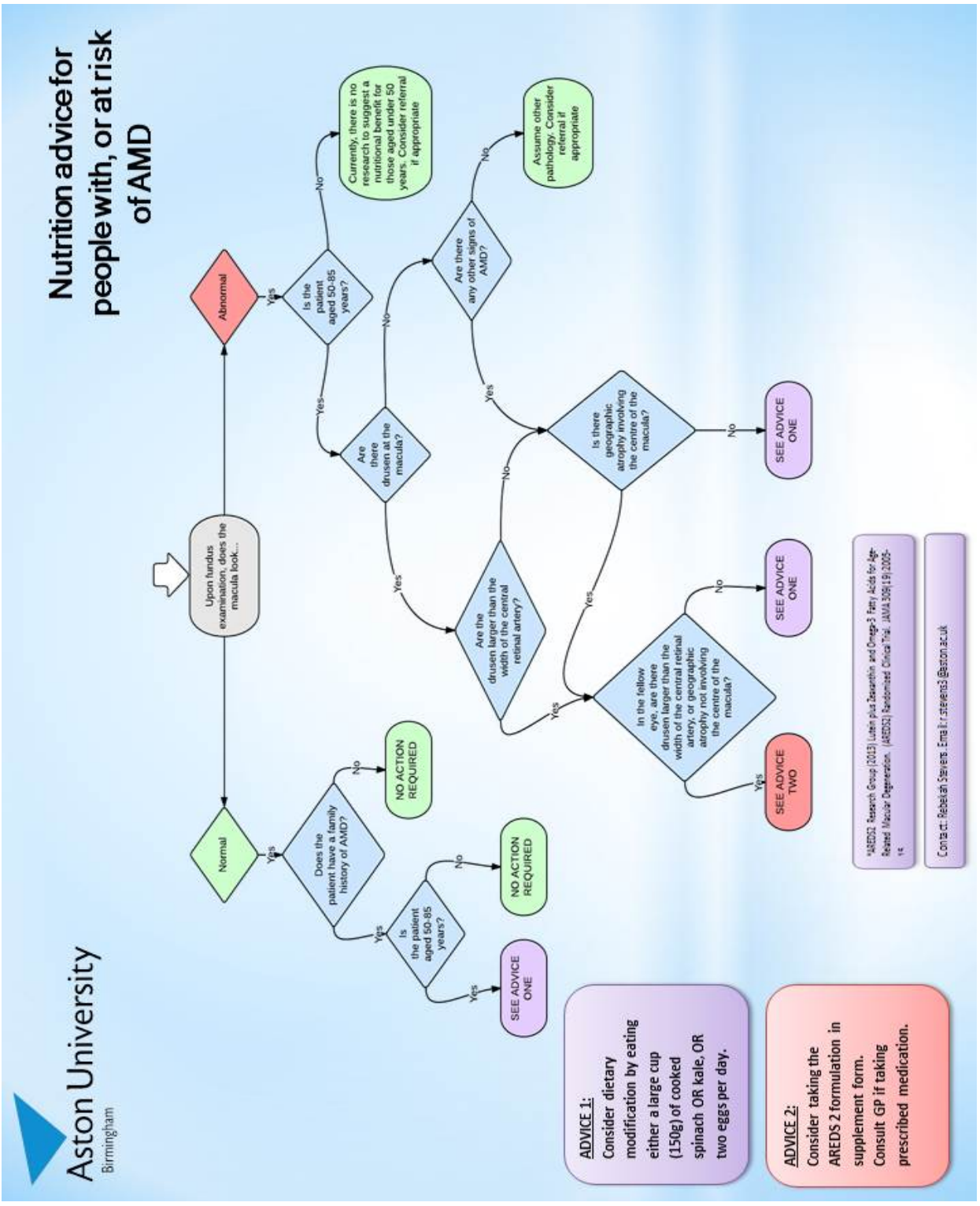


Figure 5.7. Design of the flow chart using software Lucidchart.

6.4 Pilot

As a preliminary measure, the flowchart was sent to 25 optometrists who worked in hospital, independent, multiple and university practices by email, asking for their input into the usability of such an aid. The optometrists were asked to comment on any aspect of the aid if they wished. All 25 were enthusiastic about it, and some provided useful comments about how to amend the aid to make it more user-friendly or for greater clarity. Some of the comments are shown below:

"I've had a look at the flow chart and it's pretty clear in an academic sense. If this is meant for optometrists on the high street, I think it would need a change in language to simplify it to make it more accessible as I am not convinced the average optom would understand about inclusion criteria and how studies work. Also I think it would benefit from some accompanying photos to illustrate what 'definite geographic atrophy involving the centre of the macula' etc looks like. I think the word 'definite' would also induce a sense of panic among optoms who aren't really sure and their default response may then be just to give no advice! Also when I read advice 1 quickly, it seemed to indicate a supplement plus the food. It was only on a second read that I realised it was in the food. Maybe it could be rephrased to say 'modify diet adding a cup of spinach/kale or two eggs which would provide the required 10mg lutein and zeaxanthin' or something similar?"

"The flow chart seems to be designed for patients who are not presently taking supplementation – a number of patients may be taking supplementation but, having heard about the AREDS2 study, would like advice on whether they should change.

I didn't quite follow the 'Advice 1' box as the wording implies that both the supplement and dietary elements are to be taken – does 'either with a' mean 'in the form of either a'?"

"Thanks for your email, it was really interesting. I do have a few queries regarding nutritional supplementation…Would it be a good idea to include an FAQ document along with the flow chart to help clinicians answer these?"

"Instead of stating that the patient falls out of AREDS evidence either state no current research to suggest a nutrition benefit unless there are other sources. Perhaps link people to advice 1& 2 with picture symbols"

The flowchart was then amended using the recommendations given by the 25 optometrists who piloted it (please see **Appendix 9** for the flowchart).

6.5 Evaluation surveys

The clinical decision-making aid was then evaluated using two surveys. Psychologist Albert Bandura proposed that behavioural change is linked to perceived self-efficacy - a person who believes in their capabilities to produce a given attainment is much more likely to accomplish the task[198, 199]. Evaluating self-efficacy using scales gives researchers a real idea of whether a subject is likely to accomplish a task in the future. Self-efficacy scales have been used in many surveys of medical practitioners' confidence in performing certain procedures, or giving advice to patients[200-202]. Bandura stresses the need to accurately reflect the construct when developing scales, as there is no all-purpose measure of perceived self-efficacy. The items must be phrased with '*can do*' (a judgement of capability) rather than '*will do*' (a judgement of intent), and distinguished from self-esteem [198, 199]. Using this information, a survey was created that asked participants to rate their confidence and self-efficacy out of 100 (in 10 increment steps) when performing certain tasks such as giving nutritional advice to patients, or classifying the type of AMD seen in a patient. This survey was created using the software Bristol Online Surveys (University of Bristol, 8-10 Berkeley Square, Bristol BS8 1HH, UK) (please see the survey in **Appendix 10**).

The seven item statements included in the survey were:

- I am confident that I could classify the type of AMD a patient has based on retinal signs
- I am confident that I can advise a patient with AMD on the relationship between AMD and nutrition
- I am confident that I can advise a patient with AMD on what foods to eat that might be beneficial for their condition
- I am confident that I can advise a patient with AMD on the quantities of foods that might be beneficial for their eye health
- I am confident that I can advise a patient with AMD on when nutritional supplementation may be beneficial
- I am confident that I can advise a patient with AMD on what supplements to take and what dosage to recommend
- I am confident with talking about nutrition to those at risk of AMD

These items were chosen because they cover all decisions that need to be contemplated when determining when and what nutritional advice should be given to a patient based on the AREDS 2 criteria, i.e. determining that a patient had drusen and geographic atrophy, advising a patient that AMD and nutrition are linked, determining what foods are beneficial and how much, knowing which patients require supplementation, which supplements to take (and how much), and advising those that have a family history of AMD or are at risk.

Demographic information was also elicited by questions on age, gender, number of years practising (as an eye care practitioner), the country practising in (as nutritional advice has been shown to vary in other countries [203]) , and the number of AMD patients seen each week.

A second survey was created to be filled in two weeks after receiving the clinical decision-making aid. This survey was the same as the initial survey and used the same items to rate the participant's confidence and self-efficacy out of 0 to 100 in 10 increment steps. Participants filled in the same identifying code (first three letters of the mother's maiden name, and last three digits from the postcode) in both surveys, so the surveys could be correlated.

6.6 Conclusion

This chapter has discussed the background and methods employed in the construction of a clinical decision-making aid (a flowchart) and two evaluation surveys to be used in an intervention study with qualified and student optometrists. The subsequent chapters will describe the methods used to carry out the study and the results obtained.

Chapter Seven

Qualified Practitioner Evaluation of the Flowchart

The previous chapter described the background and methods used to create a clinical decision-making aid in the form of a flowchart, and two surveys that can be used in an intervention study with optometry practitioners. For the first part of the study, qualified practitioners were used as participants. This chapter discusses the methods employed for this part of the study, and the results acquired.

7.1 Recruitment

The optometry professional magazines Optometry Today and Optician both agreed to run a 200 word feature of the study in their October issues. Readers were advised to email their interest in the study to RS, and they would receive a document with the study information.

7.2 Ethics

The procedures followed were in accordance with the ethical standards of the Aston University Ethics Committee on human experimentation that conform to the Declaration of Helsinki 1975, revised Hong Kong 1989; application number 717.

7.3 Participants

The inclusion criteria for the qualified practitioner study were that the participant was a qualified optometrist or ophthalmologist that had completed their pre-registration period. A total of 72 practitioners completed the first survey, and 46 participants from the 72 completed the second survey.

7.4 Delivery protocol

If they wished to participate in the study, they were sent a URL to the initial survey on Bristol Online Surveys where they could enter their demographic details and answer how confident they felt about the seven items prior to using the clinical decision-making aid.

At the end of the survey, a further link sent them to an Aston University website which provided them study information, with the flowchart and a list of frequently-asked-questions (see **Appendix 11, 12**) (http://www.aston.ac.uk/lhs/research/health/org/amdnutrition/).

Participants entered an email address that we could send the follow-up survey to, two weeks later. Participants were sent a URL to the final survey, where they answered again how confident they felt with the seven items after using the flowchart. If they had any other questions, they could email the researcher (three participants wanted extra clarification regarding supplements). As mentioned in **Chapter 6**, the seven item statements were:

- A. I am confident that I could classify the type of AMD a patient has based on retinal signs
- B. I am confident that I can advise a patient with AMD on the relationship between AMD and nutrition
- C. I am confident that I can advise a patient with AMD on what foods to eat that might be beneficial for their condition
- D. I am confident that I can advise a patient with AMD on the quantities of foods that might be beneficial for their eye health
- E. I am confident that I can advise a patient with AMD on when nutritional supplementation may be beneficial
- F. I am confident that I can advise a patient with AMD on what supplements to take and what dosage to recommend
- G. I am confident with talking about nutrition to those at risk of AMD

7.5 Analysis

Microsoft Excel was used to perform initial analysis; quantitative data (confidence scores out of 0-100%) was summarised using percentages and graphs. Data from Excel was then used in statistical software IBM SPSS to compare the self-efficacy between the two surveys, using paired t-tests. Chi-squared analysis was used to compare categorical data such as gender and ethnicity. An independent t-test was used to compare the ages of participants in each group, and the number of years practising.

7.6 Results

Reliability of the survey

Reliability of the scale items in the surveys were shown to be reliable: Cronbach's alpha coefficient (a measure of internal consistency, i.e. how closely related a set of items are as a group. It is a coefficient of reliability or consistency) = 0.898 for the first survey, Cronbach's alpha coefficient = 0.903 for the second survey. The mean score for the items in the first survey strongly correlated with the mean score for the items in the second score ($r=0.702$, $p<0.001$) also showing a reliable set of items.

Sample characteristics

Table 6.1 shows the number of participants completing the surveys, and the average confidence scores (derived from the scores for the seven statements). There were no differences found in the age of participants, gender or the number of years practising as an optometrist, and their mean scores of the two surveys, so these variables did not appear to influence confidence levels. Age and practising years unsurprisingly, strongly correlated with each other.

There were no demographic differences between the participants that did not complete second survey compared with the participants that did complete the second survey. The cohort of participants that 'dropped out' comprised 13 males and 12 females with an average age of 48.08 years ±11.99. The average number of years practising in these participants was 23.6 ± 12.68 years.

	Males	Females
First survey participants	38	33
Second survey participants	25	21
Confidence for first survey (0-100)	69.0 ± 18.8	70.6 ± 12.8
Confidence for second survey (0-100)	80 ± 14	84.6 ± 7.3

Table 6.1 Number of participants completing the surveys, and the average confidence scores.

Of the participants that completed the second survey, the average age was 45.22 ±11.52 years. The average number of years practising was 21.96 ± 11.73 years. Chi square tests showed no significant differences between those that completed the two surveys and gender, ethnicity, age and number of years practising.

A Shapiro-Wilk's test for normality (where p>0.05), and a visual inspection of the data's histograms, normal Q-Q and box plots showed that the male survey data was normally distributed, the female data, however, was not. The skewness and Kurtosis values for females were also outside of the +1.96 to -1.96 normal range.

Differences between surveys

Table 6.2 displays the mean confidence scores for the participants that completed both the first and second survey for each item (labelled A – G; please see item statements in **Chapter 6**, section 5.5). Both a paired samples t-test and a Spearman's rank-order correlation showed that there was a significant increase in confidence scores from the initial survey (M = 69.7%, SD = 16.2%), to the second survey after a two week usage of the flowchart (M = 82.1%, SD = 11.6%); t(45)=7.33, p=0.00), (r_s = 0.609, p = 0.00). The effect size was found to be large according to Cohen's (1992) categorisation scheme (Cohen's d = 0.88).

Confidence Statement	First Survey (n = 46)	Second Survey (n = 46)
A	72.7	80.2
B	73.9	83.2
C	76.8	84.8
D	51.3	77.7
E	66.3	83.6
F	59.3	79.8
G	70.8	86.4

Table 6.2 Mean confidence scores (0-100) for the 46 participants that completed both surveys. Confidence statements are labelled A – G (see chapter five, section 5.5).

Verbal feedback

At the end of the second survey, participants were able to write comments on the flowchart if they so wished. Of the comments that were received, the majority were very positive:

"Really useful tool particularly in conjunction with the supporting document."

"A great tool and the FAQs were useful too."

"Very simple to use and practical. Good to have a clear guide to follow. Although I knew about kale, spinach etc, I wouldn't have suggested eggs in the past.Thank you."

"nice to have clear guidelines about amounts and frequency"

"Very useful summary. Have put it up on the wall in the consulting room."

"I found this very clear, beneficial and easy to use."

Two participants included comments where the flowchart could be improved:

"Advice 1: I presume that the quantities given are to eat per day. This is not specified."

"the smallest font's too small (though my VA's fine)"

The flowchart was amended to add the wording 'per day' in the Advice One box, and the font size was increased.

7.7 Discussion

The results obtained show that eye care practitioners felt much more confident giving nutrition advice after using the flowchart for two weeks. This trend appears to be regardless of the gender or age of the participant, or number of years practising. The participants gave positive feedback about the flowchart and felt that it had enhanced their clinical practise skills.

Some participants did drop out from completing the second survey, despite having three email reminders. This could be because once they had access to the flowchart, they felt unwilling to help any further. Eye care professionals are extremely busy, and it may have simply been forgotten.

This was an opportunistic sample – we did not know how many participants would respond to the two advertisements, so we set restrictions on the time period that a potential participant could respond with interest. Funds were limited, which meant that continuous advertising was not possible. Overall, the sample size that completed both surveys was small. To recruit a larger cohort, advertisements would need to be run in a variety of professional journals

continually for a longer period of time, with larger captions (a full page spread, if funds allowed) to allow maximum exposure to potential participants.

A future step in this study would be to investigate the flowchart in action – a cohort of eye care practitioners could use the flowchart for a set period, and the patients that they see in this time could be monitored to see if they were given the correct nutrition advice, and if they put any of the advice into action.

Overall, the flowchart has proved to be a useful tool in a qualified eye care practitioner population, and by using this aid, the cohort are much more likely to be giving correct and consistent advice to their patients.

7.8 Conclusion

This chapter has discussed the methods, protocols and results obtained from an intervention study using a flowchart for qualified practitioners. The results show that practitioners appear much more confident after using the flowchart for two weeks, and are very positive about including the flowchart into their clinical practise. The following chapter will discuss the methods, protocols and results that were obtained from a study using a cohort of student optometric participants.

Chapter Eight

Student Practitioner Evaluation of the Flowchart

Aids to clinical decision making can help practitioners arrive at the correct clinical decision for patients much more efficiently. They can boost practitioner's confidence and self-efficacy in decision making, and make it much more likely that practitioners will complete a certain task. Earlier chapters have described the design and construction of an aid (a flowchart) to help eye-care practitioners decide when and what nutrition advice to give to patients with, or at risk of, AMD. The previous two chapters specifically discussed the methods and results obtained for an evaluation of the flowchart using qualified practitioners as participants. This chapter discusses the methods employed and the results acquired for an evaluation of the flowchart using a student optometric practitioner cohort.

8.1 Sample size

It was important that only students that had reached a sufficient level of knowledge about AMD were included in the study. Final year students have reached an appropriate level in their retinal knowledge to make clinic management decisions, based on the curriculum they will have covered. Aston University currently has one of the largest optometry schools in the UK, with an intake of approximately 140 students in the first year. The number of students in the final year in 2015 was 130 and as many as possible were recruited on an opportunity basis, as not all would be able to participate due to other commitments.

8.2 Ethics

The procedures followed were in accordance with the ethical standards of the Aston University Ethics Committee on human experimentation that conform to the Declaration of Helsinki 1975, revised Hong Kong 1989; application number 717.

8.3 Recruitment

Final year students at Aston University were informed about the study via email and announcements in lectures. If they wished to participate, they needed to come to the data collection session. The data was all collected in one tutorial session.

8.4 Participants

The inclusion criteria for the student practitioner study were that the participant was a registered third year student optometrist enrolled at Aston University in 2015. A total of 51 students participated in the study, 8 males and 43 females with a mean age of 21.7 ± 2.9 years.

8.5 Delivery protocol

If a student wished to participate, they attended a one-off tutorial session on the 12th March 2015. Participants were allocated to group '1' or '2' by numbering them alternatively.
Students from both groups were asked to view five pairs of retinal photos depicting hypothetical clinical scenarios of patients in various stages of AMD (see **Appendix 13**) – This type of task is similar to questions that the students will have encountered in their summer examinations. Information about the patient's age, the type of AMD they had, and if there was any family history of AMD was given underneath the photographs. The students had to then pick the most appropriate nutritional advice to give to each patient from a list of 10 possibilities:

1) No action required
2) Consider dietary modification by eating either a large cup (150g) of cooked spinach OR kale, OR two eggs every day
3) Consider dietary modification by eating either a large cup (150g) of uncooked spinach OR kale, OR two eggs every day
4) Consider dietary modification by eating either a small cup (75g) of cooked spinach OR kale every day
5) Consider dietary modification by eating 2 bananas or 2 mangos every day
6) Consider taking supplementation of vitamin C 500mg, vitamin E 400IU, lutein 10mg, xeaxanthin 2mg, zinc 25mg, copper 2mg every day. Consult GP if taking prescribed medication.
7) Consider taking vitamin C 250mg, vitamin E 800IU, lutein 1mg, xeaxanthin 5mg, zinc 250mg, copper 20mg every day. Consult GP if taking prescribed medication.
8) Consider taking supplementation of lutein 10mg and xeaxanthin 2mg every day.
9) Consider taking supplementation of gingko biloba and cod liver oil every day.
10) Refer immediately for wet AMD treatment.

For each scenario there was only one correct answer, however some of the possibilities were very close to the correct answer, while others were not. After this exercise, the participants were given a hard copy of the survey used in the qualified practitioner study (see chapter six) to fill in and measure their self-efficacy about making their decisions.

After the students had picked and marked their answers on the given sheet (which were then taken away), the groups were separated into opposite sides of the lecture hall. Group 1 were given a pack of written material about AMD – an article from Optician magazine commenting on AREDS 2 (see **Appendix 14**). Group 2 were given the flowchart developed and used in the qualified practitioner study and FAQs (see **Appendix 11**). The participants were then asked to look at the same five clinical scenarios and again pick the most appropriate advice for the patient. Once again, afterwards, the survey was administered to measure self-efficacy.

After the exercise, students from both groups were given the correct answers and both packs of information for their own studies.

8.6 Analysis

Microsoft Excel was used to perform initial analysis; quantitative data was summarised using percentages and graphs. Data from Excel was then used in statistical software IBM SPSS to firstly find the reliability of the survey using Cronbach's alpha and Pearson's correlation. Comparisons between self-efficacy levels were next performed using paired t-tests. Differences between scenario answers were found using independent t-tests. Tables were used to summarise the data and for cross-tabulation.

8.7 Results

Reliability of the survey

Cronbach's alpha coefficient was used to assess the internal consistency of the confidence scale items in the surveys. Cronbach's alpha = 0.841 for the first survey. Cronbach's alpha = 0.915 for the second survey. The mean score for the items in the first survey strongly correlated with the mean score for the items in the second score ($r = 0.503$, $p=0.012$).

Sample characteristics

Of the 51 participants, 25 were allocated in the AREDS information only group (group 1) and 26 participants were placed in the flowchart information group (group 2). **Table 7.1** shows the ethnicity of the participants. Please note, ethnicity was an open question and participants were able to write freely what they felt their ethnicity was in their own words.

Ethnicity	Participants (%)
White	17.6
Indian	15.7
Pakistani	7.8
Sri Lankan	1.9
Bangladeshi	1.9
Arab	1.9
Palestine	1.9
Asian	11.7

Table 7.1. Ethnicity information for the participants.

A Shapiro-Wilk's test for normality (where $p>0.05$), and a visual inspection of the data's histograms, normal Q-Q and box plots showed that the student survey data was normally distributed.

Confidence scores

Table 7.2 below shows the percentage confidence scores for each statement in both the first survey and the second survey, split into the two groups. Please see chapter five (section 5.5) for the specific statement items. A paired t-test showed there was a significant increase in confidence scores from the initial survey, to the second survey after receiving educational materials : Group AREDS ((M of first survey = 42.5, SD = 15.7, M of second survey = 64.8, SD = 12.3); $t(24)=7.84$, $d = 0.67$, $p=0.01$), Group Flowchart ((M of first survey = 41.7 , SD = 14.6. M of second survey = 69.1, SD = 1.7); $t(25)=7.92$, $d = 0.81$, $p<0.00$). There was not a statistically significant difference in second survey's confidence scores between the two groups, although Group Flowchart's scores were higher than Group AREDS'.

Confidence Statement	First Survey Group AREDS	Second Survey Group AREDS	First Survey Group Flowchart	Second Survey Group Flowchart
A	60.0	64.0	54.0	66.9
B	46.8	53.6	46.0	68.1
C	54.8	71.2	55.4	72.2
D	27.6	63.2	31.7	71.2
E	40.0	63.6	36.8	68.3
F	31.3	61.6	26.2	68.5
G	37.0	66.8	41.9	68.7

Table 7.2 Mean confidence levels (0-100) for the seven statements (see chapter five/ chapter six). Group AREDS had AREDS information only, Group Flowchart had the flowchart and FAQs.

Scenario questions

Tables 7.3-7.6 depict the answers given to the five clinical scenarios in the initial survey and then in the second survey according to each group. For statistical analysis, a correct answer was given a value of '1' and incorrect answers were given a value of '0'. The final value was the sum of the answers, out of a possible 5. An independent t-test showed both groups significantly increased the number of correct answers given from the initial survey to the second survey – Group AREDS $t(24)= 6.53$, $p < 0.001$, Group Flowchart $t(25)= 6.67$, $p < 0.001$. An independent t-test also showed that there was a significant difference between the two group's answers in the second survey – Group Flowchart answered significantly more correctly than Group AREDS $t(24) = 2.21$, $p = 0.03$.

Answer option	Scenario One (Correct answer f)	Scenario Two (Correct answer b)	Scenario Three (Correct answer a)	Scenario Four (Correct answer j)	Scenario Five (Correct answer b)
A	4%	8%	4%	0%	8%
B	4%	4%	0%	0%	4%
C	8%	20%	4%	0%	16%
D	8%	24%	12%	4%	16%
E	0%	4%	0%	0%	0%
F	44%	16%	36%	0%	28%
G	0%	4%	8%	4%	8%
H	8%	16%	20%	4%	16%
I	0%	4%	0%	0%	4%
J	24%	0%	16%	88%	0%

Table 7.3 Answers given to five clinical scenarios in the first survey for Group AREDS. Highlighted numbers are the correct answers.

Answer option	Scenario One (Correct answer f)	Scenario Two (Correct answer b)	Scenario Three (Correct answer a)	Scenario Four (Correct answer j)	Scenario Five (Correct answer b)
A	7.7%	11.5%	0%	3.8%	0%
B	3.8%	23.1%	7.7%	0%	19.2%
C	0%	11.5%	3.8%	0%	7.7%
D	0%	30.8%	7.7%	3.8%	23.1%
E	0%	0%	0%	0%	0%
F	61.5%	0%	46.2%	3.8%	15.4%
G	7.7%	7.7%	11.5%	0%	7.7%
H	19.2%	11.5%	7.7%	0%	19.2%
I	0%	3.8%	0%	0%	7.7%
J	11.5%	0%	15.4%	88.4%	0%

Table 7.4 Answers given to five clinical scenarios in the first survey for Group Flowchart. Highlighted numbers are the correct answers.

Answer option	Scenario One (Correct answer f)	Scenario Two (Correct answer b)	Scenario Three (Correct answer a)	Scenario Four (Correct answer j)	Scenario Five (Correct answer b)
A	0%	4%	8%	0%	8%
B	0%	24%	4%	0%	8%
C	0%	0%	0%	0%	8%
D	4%	40%	4%	0%	12%
E	0%	0%	0%	0%	0%
F	92%	12%	72%	12%	56%
G	0%	4%	0%	4%	0%
H	4%	16%	4%	4%	8%
I	0%	0%	0%	0%	0%
J	0%	0%	8%	80%	0%

Table 7.5 Answers given to five clinical scenarios in the second survey by Group AREDS. Highlighted numbers are the correct answer.

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Answer option	Scenario One (Correct answer f)	Scenario Two (Correct answer b)	Scenario Three (Correct answer a)	Scenario Four (Correct answer j)	Scenario Five (Correct answer b)
A	0%	7.6%	57.7%	11.5%	11.5%
B	7.7%	76.2%	3.8%	23.1%	73.1%
C	3.8%	11.5%	0%	3.8%	3.8%
D	0%	3.8%	7.7%	0%	3.8%
E	0%	0%	0%	0%	0%
F	80.8%	0%	7.7%	0%	7.7%
G	3.8%	0%	0%	0%	0%
H	3.8%	0%	0%	0%	0%
I	0%	0%	0%	0%	0%
J	0%	0%	23.1%	50%	0%

Table 7.6 Answers given to five clinical scenarios in the second survey by Group Flowchart. Highlighted numbers are the correct answers

Verbal feedback

After the session, a few of the participants gave verbal feedback about using the flow chart and FAQs. The feedback was all positive:

"This is such a useful tool. I wish we had more flowcharts like this to help with other conditions we are likely to see in practice".

"I would not have known where to start in giving nutritional advice, but this has made it very clear".

"We had a lecture on giving nutrition advice, but I wouldn't have known which patients to give it to - now I do".

"I like that it is small and simple".

One student pointed out that it would be useful to add in the word 'dry' to the box "Are there any other signs of AMD?" to clarify this a little more. This has since been added.

8.7 Discussion

The results obtained show that student optometric practitioners feel more confident giving nutrition advice after having specific AREDS information and after using the clinical decision-making tool on five clinical scenarios. Those that used the flowchart were more confident than those that had the AREDS information. After using the flowchart for a period of time, it would be expected that confidence levels would increase to be statistically higher than the group with just AREDS information.

The results also show that all participants chose more of the correct advice options after receiving specific information. Those that used the flowchart chose statistically more correct advice options when compared to those that had the AREDS information. It was apparent that the clinical scenario tasks appeared to vary in difficulty – scenario three had much fewer correct answers in the first survey overall (2%) when compared to scenario four (88.2%). Once the participants had received their specific educational materials, Group AREDS increased the correct responses in scenario three to 8%, but Group Flowchart increased the correct responses to 57.7% - this is a 25-fold increase. Group Flowchart appeared to have performed best at the tasks which were the hardest.

The clinical scenarios were a good method for determining increased knowledge at a specific time, and were useful as it was only possible to get the participants together once. However, it would be even more useful to see how real-life use of the flow chart would affect confidence levels – much like the qualified practitioner study.

The sample size is relatively small, as it was an opportunistic sample. In an ideal world, it would have been good to get the entire year group together, but logistically this would have been impossible as students have a varied timetable.

Overall, the flowchart has proved to be a useful tool in a student practitioner population, and students are much more likely to be giving correct and consistent advice to their patients.

8.8 Conclusion

This chapter has displayed the methods and results obtained in an evaluation study of the clinical decision-making aid using student optometric practitioners as participants. The following chapter will discuss the overall conclusions to the entire project, and discuss any future work that may be carried out.

Chapter Nine

Discussion

9.1 Main outcomes

This project sought to uncover the beliefs and opinions that AMD patients had about nutrition and AMD, and to see how these beliefs influenced their nutritional behaviour. Nutritional behaviour was contrasted and compared with a cohort of people without AMD. It was intended that a new measure of these parameters, in the form of a survey, would be designed and evaluated and could be used again in the future. The last aim of the project was to act on whatever information was gleaned from the survey in the form of an intervention - either patient centred, or a practitioner/organisation/care centred, dependant on the results found from the survey.

The nutritional awareness and behaviour survey

The survey generated some interesting data. All 158 participants could be considered an 'informed' population as they had actively sought the services and membership of the Macular Society, but all felt that they needed more information and guidance from eye care professionals, especially in the area of nutrition. Although the majority of participants were able to identify nutrient-rich foods, they were unable to verbalise why the foods were valuable for eye health, and were unsure over quantities to eat. Some 75% of the participants were taking a nutritional supplement for AMD, but were taking a variety of formulations and doses with little understanding about how supplements work. Of those that didn't take a supplement, the majority felt that supplements were not effective in slowing the progression of AMD and did not take them for this reason.

Included in the survey was a 24 hour food diary, which would provide an insight on how the beliefs and opinions of the participants manifested in their nutritional behaviour. These findings were very interesting – participants with AMD consumed an average of 1.4mg of lutein and zeaxanthin, much less than the recommended 10mg per day. Those that were not able to cook a hot meal by themselves ate significantly less lutein and zeaxanthin than those that could cook a hot meal alone. A lack of knowledge of lutein and zeaxanthin had led to a lack of consumption of these nutrients.

Participants with AMD were not consuming enough calories (average 1515 kcal) or nutrients in general – many nutrients did not reach even half the recommended daily allowance. The food

that AMD participants were eating was limited in variety, and many were not eating the lutein and zeaxanthin rich foods at all. An age-matched cohort without AMD ate an average of 1.5mg of lutein and zeaxanthin per day, and matched or exceeded the majority of the RDAs for all nutrients and calories (average 2162 kcal). Their diet was more varied, and the volume of food consumed was higher than the AMD cohort.

The reasons behind this dietary difference are likely to be multi-factorial, such as dislike for the certain foods, lack of knowledge of how to cook or prepare them, misjudging the amount required per day, or lack of control (family or caregivers cook food). Most importantly, dietary habits are difficult to change and can be quite ingrained in older adults [204]. Visual impairment itself may impact strongly on appetite, as humans enjoy the sensory experience of viewing our food before we actually consume it [179]. Visual impairment may also cause frustration when eating, and some individuals may then give up. There is very little research on the impact that visual impairment has on appetite and eating; further investigation in this area is warranted.

The Intervention

The results from the survey showed that patients with AMD would respond to more explicit guidance from eye care practitioners. Research has shown that there is variability in the advice that practitioners currently give to their patients [164], as current guidelines are vague and unhelpful. An intervention to help practitioners give consistent advice would therefore prevent patients from becoming confused, and would encourage them to take positive action to change behaviours.

A clinical decision-making aid in the form of a flowchart was created that gives practitioners clear direction as to whether supplementation or dietary modification would be appropriate for a patient, based on the inclusion and exclusion criteria of the AREDS 2 study. This aid was then evaluated using both a qualified practitioner and a student practitioner cohort, using confidence and self-efficacy scales.

The qualified practitioner cohort significantly increased their confidence scores after two weeks use of the flow chart in practice (mean = 69.9 ± 15.8% initially, mean = 82.3 ±10.7% after two weeks use), and feedback from the participants was positive. The student practitioner cohort also significantly increased their confidence scores when completing five clinical scenarios (mean = 43.4 ±10.4% initially, mean = 69.1 ± 1.7% after receiving the flow chart), and they also significantly increased the number of correct answers to each of the scenarios after using the flow chart. Feedback from the students was also very positive.

9.2 Limitations

The main limitation with the project was the number of participants recruited in each study. The number of participants in the AMD cohort was good, but it would have been more powerful to have the same number of participants in the non-AMD cohort. Many contacts in optometric practice were used to recruit, and given enough time it would have been possible – but time constraints meant that only 50 participants were recruited. To combat this limitation, a sub-group of participants with AMD were extracted that matched the age and the number in the non-AMD cohort. Their data was then used to compare and contrast with the non-AMD data.

The number of participants in the flow chart studies was lower than expected, but were still within the range calculated to show a significant effect. The recruitment for the qualified practitioner study was via two mainstream optometrist magazines with a fairly wide readership, but the adverts were quite small and could have been easily missed by many readers. Again, time constraints meant that recruitment had to be halted after three months. It was surprising that there was a number of 'drop-outs' (those that completed the initial survey but not the second) despite three follow-up emails reminding the participant to complete the second survey. This may have been due to participants only wishing to get access to the flow chart with little interest in the evaluation process. It would have been useful to recruit ophthalmologists into this cohort, and it is hoped that this group could be recruited in the future.

The number of participants in the student practitioner cohort was also lower than anticipated, but as the third year students are extremely busy in the final part of their studies, this was not too surprising. Many students expressed regret in not being able to help due to timetabling issues, and would have happily attended another tutorial session if it was set-up - the results gained from this second group, however, would not be reliable as the participants may have been already exposed to the flow chart and scenarios by the first group. As we did not know how many students would attend, and which students would attend, we were unable to randomly allocate participants to groups.

9.3 Confounding variables

Survey study

The survey was performed over the telephone thereby giving participants very little time to think about their answers, and viewpoints would therefore be less practised. As can be seen from the focus group transcription (see **Appendix 6**) however, participants seemed to be dissatisfied with their care and services available to them, which is why they were seeking the

Macular Society. To get a rounded viewpoint, patients from other organisations such as the RNIB could be included.

There were more females than males in both the AMD and non-AMD cohorts, which may be considered a confounding variable. One of the aims of the survey, however, was to reflect which patients are likely to seek the assistance of the Macular Society, and this gender difference is a finding. When viewed in this light, the gender inequality in the cohort becomes a positive aspect rather than a negative.

There is known variability when self-reporting health and visual ability [205], so it cannot be relied upon that many participants had poor vision. Information about their visual acuity would have been a useful parameter to record, but impossible due to the physical location of all of the participants. Co-morbidities may have played a role in diet behaviour, and it would have been useful to note down physical parameters such as weight, height and how physically able the participants were.

Although care was taken to note down size of portions, and participants were asked to be very specific, there will be differences in the amount and type of food recorded. The well documented under-reporting of food occurs in every age group [206, 207] , and must be taken into consideration. For future studies, we may implement a visual recording of food, such as a photo, to get a more accurate idea of portions.

Qualified practitioner and student practitioner evaluations

Confidence and self-efficacy reporting is subjective. It was felt, however, that despite the variations, self-efficacy is a more useful quality to evaluate than knowledge, as an individual may have a large amount of knowledge but poor confidence to implement it. As shown by the student practitioner study, as soon as information about a topic is read (no matter what form), confidence will increase, and this needs to be taken into account.

Confounding variables in the qualified practitioner study might have been present without the investigators realising, since the participants were taking part from across the UK with only email contact. It is feasible that participants decided to research the topic in the two-week time frame which increased their confidence. There are no guarantees that participants actually used the flow chart at all, and completed the second survey out of a sense of obligation.

The groups in the student practitioner cohort were assigned on the day, and the participants were physically spaced out so that conferring could not take place – however, there is always a

possibility that this still occurred. There is a learning effect to completing the same task again, and students may have felt more confident simply by carrying out the scenarios a second time. Since there were a lot more females in the student cohort, and confidence levels between genders can be different, it would be wise to think of gender as a possible confounding variable in this study. The clinical scenario tasks differed in difficulty – students appeared to find the third scenario much more difficult, and the fourth scenario much easier. Ideally, to get a more accurate representation of the student's decision making, the difficulty between the tasks should vary minimally.

9.4 Improvements

A longer food diary will show if the trend for AMD patients to eat less, continues. Since in this project the survey was implemented over the phone, it would have been unreliable to make participants remember what they had eaten two or more days prior to the interview. If the survey is to be carried out in the future, a longer food diary with visual recordings (such as photos) will help to investigate this trend.

Measurement of visual acuity, co-morbidities, weight, height and physical ability all may have enhanced the results obtained.

9.5 Conclusions

This project has shown that AMD patients want and need improved nutrition and diet advice from eye care practitioners. AMD patients are not consuming the beneficial nutrients to help their condition, and are at risk of damaging their general health by not eating enough food in general.

Eye care practitioners respond well to clear-cut nutrition advice guidelines, and report more confidence in giving nutrition advice when they have access to a clinical decision-making aid.

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Appendices

Appendix 1 . Good food sources of vitamin C provided by the American Optometric Association

: http://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional.

Appendix 2. Recommended dietary allowances for vitamin E, as taken from the National Institute for Health, USA Government website: http://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional.

Appendix 3. Good food sources of vitamin E provided by the American Optometric Association

Appendix 4. Recommended dietary allowances for vitamin C, as taken from the National Institute for Health, USA Government website: http://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional.

Appendix 5. Lutein and Zeaxanthin content in various foods in mole %. Mole percent, or molar percent of a substance is the ratio of the moles of a substance in a mixture to the moles of the mixture. It represents the number of moles of a substance in a mixture as a percentage of the total number of moles in the mixture. Mole % = (mol substance in a mixture) / (mol mixture) * 100 [151]

	Lutein and zeaxanthin	Lutein	Zeaxanthin	α carotene	β carotene
Egg yolk	89	54	35	0	0
Maize (corn)	86	60	25	0	0
Kiwi	54	54	0	0	8
Red seedless grapes	53	43	10	3	16
Zucchini squash	52	47	5	0	5
Pumpkin	49	49	0	0	21
Spinach	47	47	0	0	16
Orange pepper	45	8	37	8	21
Yellow squash	44	44	0	28	9
Cucumber	42	38	4	0	4
Pea	41	41	0	0	5
Green pepper	39	36	3	0	12
Red grape	37	33	4	1	6
Butternut squash	37	37	0	5	0
Orange juice	35	15	20	3	8
Honeydew	35	17	18	0	48
Celery (stalks, leaves)	34	32	2	13	0
Green grapes	31	25	7	0	7
Brussels sprouts	29	27	2	0	11
Scallions	29	27	3	0	0
Green beans	25	22	3	1	5
Orange	22	7	15	8	11
Broccoli	22	22	0	0	27

	Lutein and zeaxanthin	Lutein	Zeaxanthin	α carotene	β carotene
Apple (red delicious)	20	19	1	5	17
Mango	18	2	16	0	20
Green lettuce	15	15	0	16	0
Tomato juice	13	11	2	12	16
Peach	13	5	8	10	50
Yellow pepper	12	12	0	1	0
Nectarine	11	6	6	0	48
Red pepper	7	7	0	24	3
Tomato (fruit)	6	6	0	0	12
Carrots	2	2	0	43	55
Cantaloupe	1	1	0	0	87
Dried apricots	1	1	0	0	87
Green kidney beans	0	0	0	0	0

Appendix 6

Transcription for the survey focus group teleconference.

The reason why we have got you all together to give up your time very kindly is because any type of questionnaire based research needs some kind of validation and part of the validation process is to get a focus group of people who took part in the pilot just to find out their thoughts really. So we're just looking at how useable acceptable you found it and your general or specific feelings. Now anything that you tell me I'm not going to note down who said it so it's kind of anonymous in that way, I'm literally just going to write down and record what you are saying. Don't feel like you have to hold back in any way you can literally say whatever comes to mind even if you think it's terrible just say it, it's really important for us so then we can amend thing accordingly. Does that make sense? By the way if you need to go please do so, I'm hoping this won't take very long at all, fingers crossed it should only take a few minutes, alright that would be grand.

OK so first of all when you were approached to take part in the questionnaire did any of you feel under pressure or…

-No, no, no, no not at all

So were you asked to do it as a favour for the MDS or for Aston research group…

-I don't really remember, yes it was for the macula group and Aston society so yes anything that will help I like to do for them, for us all really.

-That's how I feel too.

Fabulous. Sorry for the delay I'm writing as you are talking, ok brilliant. So did any of you worry about your answers being anonymous or your details being known to any other party?

-No, no, no, no

Would you change any way, anything about how you were approached at all, could it have been done in a better way?

-No, no, no it was fine, I don't see how any other way is possible you know

I think how it will be done is probably via the help line people will be asked if they would like to take part in the research and if so we'll take their details and call them back at a later date, the option is that we could complete it there and then but I think it's better to go back to it when the patient has had time to think about it which is what happened with yourselves, if you wanted to opt out then you could have done at that point.

-I preferred someone to come back to me.

-When you say via the helpline what do you mean? If someone rings the helpline up they might be asked if they want to take part?

Yes, what do you think about that?

-Well if they ring the helpline they're probably in need of help rather than being asked to do some research. I thought you meant the helpline would ring people that belonged to the society.

Well I think that's going to happen as well.

-Could you not put something on the website?

We can yeah.

-Everybody doesn't have a computer.

-No but they only need a few people.

-But still yes you need a cross section

-How many people are you thinking of?

-In my MD group the majority don't have computers but I'm sure they'd be very good to do research on about whether they're getting the nutrition they should be getting.

-Or you could actually send out a letter to all the groups.

-Yes that might help

-Then they could do their own survey within their group

-But then I could have a problem with the York group because they're not really affiliated to the macular society, the York blind and partially sighted society who started this group about 30 years ago I think but they don't get letters unless the chairman is a member of the macular disease society, a lot of them aren't members we try and get them to but they won't.

-That's the same with Barnet's in London, The Barnet's Sight and care group, whereas we do get the literature only a handful of us belong to the society. I'm sure they'd be willing to take part.

-I think they would yes but they don't need to be part of the society to take part.

-No they don't but I was just getting the information across.

-I know yeah.

-I suppose it would have to be someone like me who goes to the society or group to tell them. But I'm not sure I like the idea of if someone has a problem, rings the helpline being asked if they would do something.

-Yes I agree.

-Thinking of what I was like when I first had it.

OK

-I think from my point of view my own support group would be very happy to have a phone number and if they wanted to take part to give someone a ring and put their name down as it were and get someone to ring them back.

Righty ho.

-That's an idea we could always do that with any of the groups couldn't we.

Brilliant, good, thank you. So did the questionnaire take up as much time as you expected or did you expect it to be longer or shorter, I know I chatted a bit.

-I've no idea I was recovering from a shoulder operation.

-About 20 minutes was it?

-Yes it was

-Yeah it was long enough

-Anything longer too long

Now were you happy to chat or would you have preferred the questions to more succinctly put?

-I'm always happy to chat

It's not a general consensus, I'll note down what everybody says

-I was quite happy the way it was

-As long as we didn't take too much of your time I suppose

It's my job.

-Could I ask about the point where you are contacting other people about their nutrition etcetera are you always going to do it on the telephone? Or is there any other way you are going to contact people?

Do you mean when we contact them to take part?

-Yes

When we're actually doing it, it will have to be consistent so it will have to be telephone. So what we're planning to do is the survey itself will be uploaded to a website but the subject isn't actually going to do that themselves, we are going to have a volunteer, I think it's possibly Tom who is listening in at the moment who will be filling in that survey for them via the phone.

-Aha yes makes sense I was just wondering how people were going to get the stuff down.

Yeah it's difficult because you have to vary your questionnaire according to the method in which you are deploying it.

-Yes I know, I've done this before.

So if we can keep it consistent I think that's the general idea. OK, so the initial questions were what we would class as demographic questions finding out a little bit about you, did any of you find them intrusive at all?

-No, no, I can't remember what they were

Things like your age, who you live with, what type of accommodation you are in and what your occupation is essentially

-No didn't worry me, just wondering why it was relevant what type of accommodation you were living in, I thought it was going off the point a little.

-I thought it was if we needed help, how we managed in the house

It is about trying to link in certain questions, if somebody was living in sheltered accommodation they might be having their meals sorted for them and we would be asking that later on, so what they answered earlier would change what I asked later on. It's for that reason, also when we try to do the statistical analysis it's to put people into different groups, but we don't want it to be intrusive.

-Could you say a little bit at the time why you are asking that question?

We could do yeah

-I thought you were just asking about the welfare of the person you were speaking to, I remember saying I'd just had this operation and I had all the food in the freezer and I was fine.

It is partially that as well

-There are some people who aren't able to do that.

Yes absolutely

-I trusted it because it was the macular society and you were from Aston University and it was a good thing. But I get a bit annoyed when its people who are cold calling and they ask what sort of accommodation you are in, those times it can be intrusive. This was only OK because of the background.

-I tell them I live in a tent

It would be better to have an explanation bit in there

-But it's not cold calling

So the next bit of the questionnaire was about the type of AMD or macular issue you had. Did any of you mind answering that?

-No, no, no. Taking part in a survey you've got to expect to answer questions.

Would any of you think that the general public might not know the types of AMD, they might just have been told they have AMD.

-Yes that happens

-I had it all explained to me, depends who your consultant is and what the nurse tells you I suppose.

-I'm a group leader and I know people often don't know what type they've got

-It's becoming rarer because opticians are much more aware of MD and they've got the stuff in their consulting rooms, but I've been doing this a few years now and I see more and more people coming and they know whether they have wet or dry, but there's just the odd person

-Sometimes they don't know because they haven't taken it in

-Sometimes it takes time to diagnose, it took 10 years for myself, and someone I was talking to the other day, he's not been diagnosed and he's in his 50s

-It's because they don't expect you to have it

-Yes, it can be very rare

-And it can be combined with other things

Good to know

-We're getting better I find, at hospital they answer questions but not everybody likes to ask. They're in shock at the time I think. They can't formulate a question.

-At our hospital there isn't room for carers to sit with them, they do about 60 a day and they come out a little bit bewildered some of them at times, that's when I trot up and down the line, but I only go once a month.

What did you think about us asking about the visually impaired register? Was that something any of you minded being asked?

-No, I think it's important to know who's actually registered

-A lot don't want to register, I find there's a lot who don't want to register

-You know why don't you?

-They can't drive, that's why they hang on until the last minute

I had a whole section which I think some of you didn't actually answer because you answered differently early on about cooking and preparing food. I did have some options about who mostly cooks and who mostly prepares food and the options were yourselves, your partners, your family members and your care givers. Is there anybody else I could have included?

-Meals on wheels, you might have to include where the meals come from.

-I get Wiltshire farm foods. There's another firm but I don't remember the name. I only do that because of my shoulders, not because of my eyes.

-Could you include an open question?

I was just checking I hadn't missed a major category

-I live out in the country and there's a lot of young people who like to cook and freeze things and they pop round and say "We're cooking do you want anything?"

-That's lovely, but what do you call them? Preparers or helpers?

-We pay for it

-Don't think you'd get that in our area

-Nor mine

-What would you call them, that's what I was meaning

Paid assistance maybe? I'll put some thought into that.

Now I've got a list of reasons for people not being able to cook or prepare food, and I'd got visual impairment, physical impairment or other. Anything else I should have put in there?

-No, physical and eyes are about the only things

I then asked you all about what you ate yesterday, did any of you find that difficult to do?

-No, sometimes I have to think, but if I really concentrate then no.

Now we found a huge variation on the amount of detail you provided, would it be useful for you to just say whatever you wanted or should I have been a little more explicit with what I said?

-I just wondered what was the point of the survey. Was it in general to find if people of a certain age aren't able to care for themselves therefore their nutrition isn't adequate at this time in their life or is it in their history, what was their diet like as a child, any absorption problems or have they avoided any food because of allergies or they didn't like them. In a way I didn't think it was specific enough with foods that may be good for you you have avoided throughout your life for whatever reason and have a common link or you have macular disease because you've had a bad diet from fifty onwards. I'm in my fifties and I've had this since my forties so it's my diet in my twenties or as a child that has affected it now. In a way I thought it was too general, the questions.

So this timeframe is too small?

-Yes I wish you had gone back to childhood. The only complaint I had is that the society did a survey looking at diet, absorption and ulcerative colitis, it would be good if someone went through all the foods we are avoiding, for example I never ate any eggs and I am wondering if

eggs are very good for you then that's probably why my eyes are very bad. That's just one example and in a way I'd like it more specific.

-I think so, if they're really going to go into the nutrition bit a lot of us who are in our eighties can go back to what we had during the war. It's a very big subject.

-On the other hand you can't say if you were deprived of certain things during the war maybe that's a reason for macular degeneration. I used to smoke in my student years and some lady said to me that's why you've got macular degeneration. That might be but as regards our condition there are all sorts of things that might come in that will cause it not necessarily lack of certain foods.

-And also you didn't ask whether it was in the family either.

-But you wouldn't have known way back because it wasn't diagnosed.

So asking about AMD in the family.

-If that's what you want as regards your nutrition survey. You may not want to know that.

It's all up in the air really, its trying to work out what's going to give us the best unbiased view and what to leave in and what to take out, but we don't want it to be too longwinded, bit of a toss up really.

-Everyone thinks they have a good diet until things are pointed out to them.

-It's just AMD you are surveying not the dystrophies?

No technically it's just AMD, I know we bent the rules just for yourselves but for the official survey it will just be AMD.

-Might be useful then to ask what their diet was like or had they had any illnesses as well like ulcerative colitis or Crohn's disease where you are not having full absorption.

So it would be useful to pop in a general health question.

-Can you just say quickly what is the point of it? What is it about? I know it's about nutrition but what are you trying to do?

We are trying to find out if people are being given enough information about nutrition from the practitioners point of view but also whether there's a case to show patients with AMD find doing that nutritional advice difficult. So if people are told to eat kale but have difficulty preparing it should we be doing something else.

-Like supplements

-Really then what they've had in their past life is irrelevant.

Sort of yes, but it is important to know the type of subject we are dealing with. So someone who is in their fifties and suddenly develops AMD and someone in their eighties who has had

AMD for some time that goes wet, we would want to see the differences between the two, so putting in a general health question would probably be quite good.

-When people get older sometimes they can't be bothered to eat properly

Yeah we've got to find that out, is it their eyes or is it other factors

-You want to see how different is their diet, whether they are taking all this stuff the kale and egg yolks are you wanting to know if they are doing that is it making a difference

-You wouldn't be able to tell that

You couldn't do that on a questionnaire, its more about how patients are feeling themselves, are they being given advice and then are they able to put that advice into practice or is that advice redundant because of their condition, its almost like a chicken and egg situation

-I don't think they're given advice through the hospital are they?

That's the thing we need to find out

-Well I was but I think my consultant was a bit of an exception

I asked everybody about a list of foods, carrots, spinach, ice cream and whether it affected eye health and we were thinking of asking why you thought it affected eye health. Do you think that would be a good idea or would it be too hard for some people?

-Why do we eat these foods? Probably because we've been told at a conference that these foods are beneficial for people with AMD. I wouldn't have had kale unless I had been told specifically because it wasn't available at one time. Now it's much more available. Whether that's through the macular disease society I don't know. I think people who have been to the conference and listened to people talking about nutrition and bought a cookbook, I don't think other people would be aware of these foods.

-But we have the macular booklet A51 which is good and feel we have it drummed into us and if you are part of a group you probably know these things.

-There are those who want to hear and when I chat to people they don't even know there is a macular disease society. The problem is there is a table but everyone has drops in their eyes so they don't read it. There's not enough room for carers so they are in the wrong place. A lot I talk to don't even know there's a group.

-My consultant has help cards with a number on, he gives those out.

I talked about nutritional supplements and it occurred to me that someone in the general public might not know what a supplement was. Is that something you've come across in your groups?

-No, but it is possible I suppose.

-I think it would be good to put something about lutein and antioxidants in it.

Define it a little better then?

-Maybe they could have a questionnaire handed to them by whoever is looking after them in the department just to say do you eat this and do you take that supplement. Would that be any good?

-It's very difficult there's lots of bits of paper on the chairs but everybody sits on them. They don't pick them up because they've got the drops in.

I also asked at the end how much money people would be willing to spend on a nutritional supplement that would be useful for them, and why they would be willing to spend it. Is that a good idea?

-Yes.

We added the why so we could find out if it was their personal income or the nutritional supplement.

-If they're going to work I probably would but there's no guarantees.

-Surely there's one supplement you can get on the national health.

-My doctor won't give me mine now.

It's very variable. I think everyone is waiting for the AREDs study.

Would you have liked a section about AMD to express your thoughts about how much information is given and we jotted down your thoughts, would that be a good idea? Or would you prefer to say how you feel about certain statements?

-Is that really relevant to your study about nutrition?

-It would make your questionnaire far too long because some people have issues and would go off on a tangent.

-How would that be useful to you?

It's all part of qualitative analysis which lets the subject tell you exactly what's on their mind and sometimes gives you a better idea of their thoughts rather than try to restrict them into a certain category. It's harder for the person collecting the data but at the end it can be more useful.

-If it's useful give people an opportunity if they wish.

-Can you record it?

We don't know yet, we have to fill in ethical applications.

-I think you'll get a lot of response because there's a big gap from when they're first diagnosed and what happens to them. There's no continuity, it's just here you go, goodbye and they leave the consulting room shocked, angry and thinking now what happens, and they are turned out on the street and sort yourself out. There's a lot of anger and this will all come out.

-If the social worker is not at the hospital at the time they're not guided to ask her any questions. I think that would be a good idea but then you've got to get up to the staff and consultants and get them a leaflet to take home for them or their carer to read.

That was all the questions I had for you, I would just like to know if there's anything else you would like to change in the questionnaire or point out any flaws or anything else you can think of and I will make a note of them.

-When you've done this questionnaire and got it all assimilated do you send it to the ophthalmologists?

No it's probably going to form part of other research and may branch into something else. Eventually though it will get published and ophthalmologists and opticians will be able to see it. We were thinking of doing an advertising campaign of what we are doing but it's all up in the air until we know what our data is.

-I think an advertising campaign would be useful as people don't realise what you can see and what you cannot see and why, and people think oh you're blind. Make people aware that eye problems exist and because you can see something you're not fine, and correlating some of your information to the healthcare workers but there's big gaps in how they work because it's not in their job description, pointing out where they can help.

-Everybody's different in what they can see with AMD.

-People who can see might then be aware of what it's like with AMD, and even having a bit more understanding when somebody stands next to you and asks you to read something they don't give you a double take "Woah that's big enough can't you see that". Some people have sight problems and don't have a sign on top of their heads saying I have a sight problem.

-I have to say I can read but I can't see it.

-You have to justify everything and that's what annoys me.-The badges we wear, people don't like wearing badges. A lot of people who can see don't know what it is anyway.

Any other thoughts with regard to the questionnaire?

-Why did you ask about ice-cream?

A lot of people will correlate carrots with eyes because that's what they've been taught. Putting a bit of a curve ball in like cheese and ice-cream it's to filter out people who would just say yes to anything.

-But with the ice-cream and the cheese I think fats are good with the anti-oxidants because they absorb better, I thought that's why you put the cheese question in.

Not necessarily, but we want to know why people say yes to why they affect the eye.

-So are you going to say anything about the needs for fats with anti-oxidants?

We are not going to comment in any way.

-Not even at the end of it? Things like the omega oils are good.

With regards to nutrition that is good for AMD it is literally just the antioxidants. Lutein and the things that you would find in kale and chard and that sort of thing, I put mango down and that is not particularly useful although people assume it is. There's a lot of variability and we wouldn't even comment at all even at the end of the questionnaire, we would refer the patient back to the MDS for the information.

-I've taken antioxidants for ten years and I've still got it.

-With all these things there really is no proof.

Everyone's waiting for the AREDS study for guidelines.

-I think it's been proved about the lutein though hasn't it.

That's why lutein injections are given.

-Ooh do they do lutein injections?

Yes the issue is capturing at a certain stage of the AMD before treatment can be done.

-I was talking about lutein not lucentis!

Oh sorry.

-Lutein spray, capsules, by mouth.

It's about trying to do as much as you can, for some people it's good and for some people it's not so good. It's kind of luck of the draw. It's worth a go for many people.

-Anything's worth a go.

-Then there's sunlight as well isn't there

Well that's it at the end of the questionnaire I asked about smoking. I think what we will do is not give the categories out at all just ask them what behavioural or conditional factors affect. Anything else ladies?

-Sorry I have to go, is that it?

Yes, that's it. I'm really really grateful. Is there anything that Tom or Andy or Pete want to add at all

-No

-I don't think so Rebekah

Fabulous, thank you very much.

-There is one thing, I wondered if your sample gets the opportunity to get your research results?

Tentatively yes everyone gets the chance, I'm not sure how that will be distributed. We will definitely make the results known to MDS, but whether we get everyone who took part and give it them might be a different matter. What we might have to do is provide a contact number or email for them to come in themselves.

-Webpage?

-Publish in the magazine?

Yeah that's the other thing the MDS magazine would be useful.

-Even a more in depth one in digest.

-Yes

-I think that's a good idea and I'm sure that will be done.

Thank you I'm really grateful. This is an important part of the validation process. This focus group has made it more valid. Hopefully we won't have to bother you again.

-Bye

-Bye

-Bye everybody

51.53, focus group have left conference

Appendix 7. Final survey.

Questions	**Options**
How old are you?	
Would you describe yourself as…	Male
	Female
Do you live…	Alone
	With partner
	With family
	With friends
	Other (please specify)
Do you live…	In own residence
	In family/ friend's residence
	In sheltered accommodation
	In nursing home
	Other (please specify)
What is, or was your main occupation	
How would you describe your general health today? How would you describe your vision today?	Extremely good
	Good
	Satisfactory
	Poor
	Extremely poor
Do you have the eye condition age-related macular degeneration	Yes
	No
	Have not heard of this condition
If Yes, how many years have you had it in total?	
What type of age-related macular degeneration do you have?	
Are you on any visually impaired register?	Sight impaired (partially sighted)
	Severely sight impaired (blind)
	Neither
Who MOSTLY prepares your food?	You
	Partner
	Family member
	Care giver
	Other (please specify)
Who MOSTLY cooks your food?	You
	Partner
	Family member
	Care giver
	Do not eat cooked food

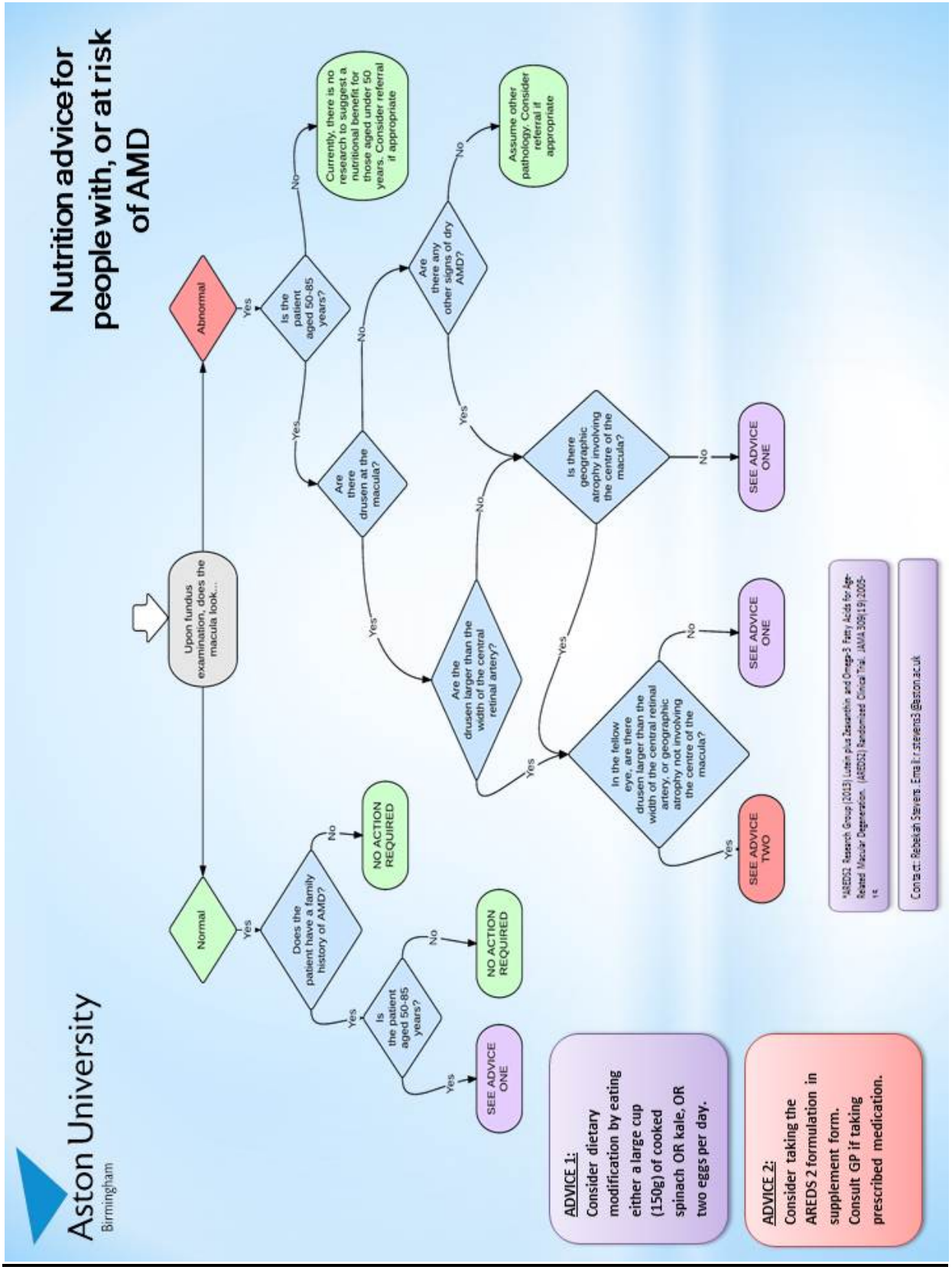
	Other (please specify)
What prevents you from preparing food (select all that apply)	Visual impairment
	Physical impairment
	Nothing
	Other (please specify)
Are you able to cook a hot meal on your own?	Yes
	No
What prevents you from cooking food (select all that apply)	Visual impairment
	Physical impairment
	Nothing
	Other (please specify)
Who MOSTLY does your food shopping?	You
	Friend
	Family member
	Care giver
	Other (please specify)
Where do you get your food from? (select all that apply)	Supermarket
	Local grocers/ corner shop
	Internet
	Meals on wheels
	Market
	Grow own food
	Other (please specify)
What is the most important factor that dictates what you eat?	Cost
	Preference
	Habit
	Ability to cook or prepare it
	Ability to acquire it
	How it affects your health
	Other (please specify)
Would you like to change your diet in any way?	Yes
	No
What prevents you from changing your diet?	Visual impairment
	Physical impairment
	Nothing
	Other (please specify)
	Do not want to change diet
Please could you describe what you ate yesterday (Breakfast, Lunch, Dinner, Snacks - your interviewer will describe portions).	
Were the vegetables eaten yesterday (if any)…	Mostly cooked
	Mostly raw

	No vegetables eaten yesterday
Please state how strongly you agree or disagree with the following statement:	Strongly agree
There are specific foods that can affect your health.	Agree
	Neither
	Disagree
	Strongly disagree
Please state how strongly you agree or disagree with the following statement:	Strongly agree
There are specific foods that can affect your EYE health.	Agree
	Neither
	Disagree
	Strongly disagree
Do you think any of the following foods are beneficial for eye health… and why	Carrots
	Ice-cream
	Spinach
	Cabbage
	Kale
	Bilberries
	Cheese
	Peppers
	Mango
Which, if any, of the following vegetables did you eat last week? (select all that apply)	Carrots
	Peas
	Spinach
	Cabbage
	Broccoli
	Kale
	None of the above
Have you ever discussed taking a nutritional supplement with a health specialist or advisor?	Yes
	No
If yes, who?	Ophthalmologist
	GP
	Optician
	Specialist doctor
	Nurse
	Herbalist
	Pharmacist
	Dietician
	Helpline worker
	Other (please specify)
Do you Currently take any nutritional supplements?	Yes

	No
If yes, what supplements do you take?	
How often do you take the supplements listed above?	More than twice per day
	Twice per day
	Once per day
	Once per week
	Other (please specify)
If you answered No, Can you give a reason for not taking a nutritional supplement	Too expensive
	Not sure if effective
	Fear/ experience of side-effects
	worry about interaction with other drugs
	Too much trouble
	Other (please specify)
How much money would you be willing to spend on a monthly basis on a nutritional supplement which promised good results?	No money
	£1-5
	£6-10
	£11-15
	£16-20
	£20+
Please state how strongly you agree or disagree with the following statement:	Strongly agree
Age-related macular degeneration patients are given enough information on how nutrition affects their eye health.	Agree
	Neither
	Disagree
	Strongly disagree
Where have you received information on age-related macular degeneration from? (select all that apply)	Opthalmologist
	Optician
	Internet
	Newspapers
	TV
	Organisations such as the Macular Society
	Other (please specify)
Do you believe that age-related macular degeneration can be prevented by lifestyle choices such as nutrition?	Strongly agree
	Agree
	Neither
	Disagree
	Strongly disagree
Which changes to the way that you live do you think could affect age-related macular generation?	

Appendix 8 –Example of a flowchart used in optometry is the US to help aid diagnosis with low vision patients from http://www.odcareer.com/bad-vision/

Appendix 9. Final flowchart.



Appendix 10. Qualified Practitioner Survey

1. I confirm that I have read and have understood the information for the above study and have had the opportunity to ask questions via email.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.

3. I agree to take part in the above study.

4. Please tell us the first three letters of your Mother's maiden name

4.a. Please tell us the last three digits (one number and two letters) of your postcode

5. Please provide a valid email address below. This will be used to send a link to a follow-on survey.

6. How old are you?

7. Would you describe yourself as... Male or Female

8. How many years have you been practising as an eye care clinician?

9. On average, how many patients with AMD do you see per week?

10. Which country do you currently practise in?

11. Please state your ethnic background

12. Please select an option for each row of the table to indicate the degree of confidence you feel for each of the following statements:

	Select you level of confidence from 0 - no confidence, to 100 - highly confident										
	0	**10**	**20**	**30**	**40**	**50**	**60**	**70**	**80**	**90**	**100**
a. I am confident that I could classify the type of AMD a patient has based on retinal signs	●	●	●	●	●	●	●	●	●	●	●
b. I am confident that I can advise a patient with AMD on the relationship between AMD and nutrition	●	●	●	●	●	●	●	●	●	●	●
c. I am confident that I can advise a patient with AMD on what foods to eat that might be beneficial for their condition	●	●	●	●	●	●	●	●	●	●	●
d. I am confident that I can advise a patient with AMD on the quantities of foods that might be beneficial for their eye health	●	●	●	●	●	●	●	●	●	●	●
e. I am confident that I can advise a patient with AMD on when nutritional supplementation may be beneficial	●	●	●	●	●	●	●	●	●	●	●
f. I am confident that I can advise a patient with AMD on what supplements to take and what dosage to recommend	●	●	●	●	●	●	●	●	●	●	●
g. I am confident with talking about nutrition to those at risk of AMD	●	●	●	●	●	●	●	●	●	●	●

Appendix 11 - Clinical decision-making aid FAQs.

Aston University
Life & Health Sciences

Nutrition Advice for people with or at risk of AMD

Frequently Asked Questions

Why is AMD research important?

Age-related macular degeneration (AMD) is the leading cause of visual impairment in older adults in the developed world (1). As the population increases and people continue to live longer, finding ways to reduce the risk of onset and progression of the condition is imperative.

What risk factors are associated with developing AMD?

There have been many studies into risk factors associated with AMD. These include age, gender, genetics, UV light, smoking, light coloured irises, hyperopia, race, BMI and obesity, alcohol, cardio-vascular disease, statins and some hypertensive medication (2). Many studies have been concerned with investigating the density of macular pigment at the macula. Macular pigment is made up of lutein, zeaxanthin and meso-zeaxanthin, and these carotenoids collectively protect the macula from oxidation and blue light which are thought to be involved in the development of AMD. Macular pigment is acquired purely from our diet. Some studies have shown that the density of macular pigment is lower in those with AMD.

Which foods contain lutein and zeaxanthin?

The largest amount of lutein and zeaxanthin can be found in kale, spinach, eggs and goji berries. Other leafy green vegetables, peppers and some fruits also contain the carotenoids, but with lesser amounts. To impact on the macula pigment, 10mg of lutein and 2 mg of zeaxanthin ingested per day has been found to be beneficial (3). This can be obtained by eating only two eggs OR a large cup (150g) full of cooked spinach OR kale per day (4).

A patient might feel that these foods are not to their taste and would rather have a nutritional supplement instead. There is positive research to support supplementation in patients with intermediate to advanced AMD – the clinical decision making aid will enable you to decide whether a patient falls into this criteria. There are currently many eye supplements available, and there have been many studies into various formulations of supplementation – the largest trial of recent years is the Age-Related Eye Disease Study (AREDS) based in the US.

What is the Age-Related Eye Disease Study (AREDS)?

The world's largest clinical trial into dietary supplementation for AMD was first conducted in 2001. The follow up trial study (AREDS 2) released their results in 2013. The team initially investigated a combination of high dose nutrient supplementation on AMD and cataracts over a period of 6 years. The AREDS formulation of vitamin C 500 mg, vitamin E 400 IU, b-carotene 15 mg, and zinc (zinc oxide 80mg and cupric oxide 2 mg) showed a 25% risk reduction in progression to advanced AMD over 5 years in patients with intermediate AMD (extensive intermediate drusen in one or both eyes, one or more large drusen in at least one eye, or nonsubfoveal geographic atrophy in one eye) or advanced AMD (subfoveal geographic atrophy or choroidal neovascular membrane) in one eye (5). The risk of losing vision of three or more lines also was reduced by 19% with this combination treatment. Because of the high dosage of zinc, and the inclusion of beta-carotene, some ophthalmologists and other eye professionals became concerned with the safety of the formulation and were reluctant to advise patients to use it.

A further study (AREDS 2), which encompassed lutein and zeaxanthin to the original AREDS supplement formulation, found that using lutein and zeaxanthin instead of beta-carotene further reduced the risk of progression to advanced AMD by 18%. The dose of zinc was reduced in this new formulation (3).

What advice can practitioners provide for patients who have, or are at risk of, AMD?

Currently, the advice that practitioners provide patients can be vague. The College of Optometrist's guidelines state that patients should "eat leafy green vegetables". A recent study into AMD patient's nutritional behaviour showed that the majority of AMD patients felt confused by the information given to them, and many reported that they needed much more guidance (6). Patients are also overwhelmed by the number of eye supplements on the market – many of which have no clinical evidence to support them.

By using the AREDS 2 study as a guideline, practitioners can be more unified in giving nutritional advice to patients with the confidence that the advice has been rigorously investigated. The clinical decision-making aid is designed to help decide which advice to give – supplementation and/or diet modification, labelled as 'Advice 1' and 'Advice 2'.

Advice one refers to dietary modification – the patient can incorporate 150g (one cup or one large handful) cooked spinach or kale, or two cooked eggs into their diet. These can be eaten either alone or part of a recipe. Advice two refers to supplementation - the supplement type can be narrowed down to the AREDS2 formulation, the details of which ones are shown below.

Can a simple balanced diet provide 10mg of lutein and 2mg of zeaxanthin?

Incorporating some leafy green vegetables such as cabbage and broccoli will provide the body with some carotenoids. However, standard portions of many vegetables and fruits will not provide the recommended 10 mg lutein. Examples of the amounts of lutein available in different foods can be found in the table below. Please note that lutein and zeaxanthin are extracted from foods together, so a small amount of zeaxanthin will be incorporated with each 10 mg portion of lutein.

Are two eggs per day safe?

FOOD	SERVING SIZE	LUTEIN (mg)
Kale, cooked	1 cup	20.5
Collard greens, cooked	1 cup	15.4
Spinach, cooked	1 cup	12.6
Turnip greens, cooked	1 cup	12.1
Broccoli, cooked	½ cup	4
Spinach, raw	1 cup	3.6
Aubergine, raw	1 cup	2.6
Peas, cooked	1 cup	2.2
Broccoli, raw	1 cup	2.1
Corn, cooked	½ cup	1.5
Lettuce, cos or romaine	1 cup	1.5
Brussels sprouts, cooked	½ cup	1.1
Papaya	1 papaya	0.3
Peaches	1 peach	0.2
Apple	1 apple	0.04

Up until recently, eggs have been linked to increased cholesterol and the Food Standards Agency's advice was to limit consumption. However, this advice has now been altered and now consumption is unlimited. The guidance for older adults is to make sure the egg yolks are fully cooked to avoid risk of salmonella poisoning (7).

What is geographic atrophy?

Geographic atrophy can be defined as a demarcated circular shape at the central macula, with reduced retinal pigment epithelium. Please see the diagram.

Diagram available from www.myvisiontest.com **Why do the drusen need to be larger than the central retinal artery?**

As we are only able to give advice based on the exact AREDS2 inclusion criteria, supplementation can only be recommended if the drusen are larger than 125µm. Since this is a difficult size to evaluate, we have used a retinal marker to help gauge the size. The average central retinal artery can vary between 140 - 170µm, and so underestimation of drusen is unlikely by using this retinal marker.

Where can a patient get an AREDS2 supplement?

To date, there are few supplements that are 'pure' AREDS 2 formulations, and contain nothing but the following ingredients:

Lutein = 10mg Zinc = 25 mg

Zeaxanthin = 2mg Copper = 2 mg

Vitamin C = 500mg Vitamin E = 400IU

Viteyes® by Butterfly Healthcare is a pure AREDS 2 formula – please look around for other brands that might emerge in the next few months. There are other supplements that are very near to the AREDS2 formulation that you might also wish to consider, such as EyeBar®, MacuLEH® and Macushield Gold® - these contain the necessary AREDS 2 ingredients, but they might also contain extra carotenoids or ingredients such as omega3 or meso-zeaxanthin, and reduced amounts of copper.

What are the risks associated with taking the AREDS2 supplement?

There are currently no known risks with taking an AREDS2 supplement. Having the correct dose is very important, as some AMD patients do not realise that there is no increased effect by double or triple-dosing. Please refer to the specific supplement for dosing information, as they can vary between brands. It would be wise to advise a patient to inform their GP when taking supplements as there may be interactions with prescribed medication.

1. Owen CG, Jarrar Z, Wormald R, Cook DG, Fletcher AE, Rudnicka AR. The estimated prevalence and incidence of late stage age related macular degeneration in the UK. BRITISH JOURNAL OF OPHTHALMOLOGY. 2012;96(5):752-6.
2. Berrow E, Bartlett H, Eperjesi F, Gibson J. Risk Factors for Age-related Macular Degeneration. European Ophthalmic Review. 2011;5(2):143-53.
3. Chew EY, Clemons TE, SanGiovanni JP, Danis R, Ferris FL, Elman M, et al. Lutein plus Zeaxanthin and Omega-3 Fatty Acids for Age-Related Macular Degeneration The Age-Related Eye Disease Study 2 (AREDS2) Randomized Clinical Trial. JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 2013;309(19):2005-15.
4. Vishwanathan R, Goodrow-Kotyla EF, Wooten BR, Wilson TA, Nicolosi RJ. Consumption of 2 and 4 egg yolks/d for 5 wk increases macular pigment concentrations in older adults with low macular pigment taking cholesterol-lowering statins. American Journal of Clinical Nutrition. 2009;90(5):1272-9.
5. Kassoff A, Kassoff J, Buehler J, Eglow M, Kaufman F, Mehu M, et al. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Archives of Ophthalmology. 2001;119(10):1417-36.
6. Stevens R, Bartlett HE, Walsh R, Cooke R. Age-related macular degeneration patients' awareness of nutritional factors. British Journal of Visual Impairment. 2014;32(2):77-93.
7. Food Standards Agency http://www.food.gov.uk/multimedia/faq/lascaloidfaq/lascaloidqa07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Appendix 12. Qualified Practitioner Study Information

Aston University
Life & Health Sciences

STUDY INFORMATION

Nutrition Advice for people with or at risk of AMD

Purpose of the study

Age-related macular degeneration (AMD) is the leading cause of visual impairment in the western developed world. Marketing of nutritional supplements towards people with, or at risk of, AMD has made it very difficult for patients and eye care practitioners to determine what nutritional advice to follow. Despite the wealth of supplements that are available, only two formulations are backed by large-scale clinical intervention trials. These are the AREDS 1 and AREDS 2 formulations (we have focused on the more recently developed AREDS 2 formulation). Even armed with this information, patients and practitioners need to know which patients meet the AREDS inclusion criteria, and so could benefit from this specific formulation.

We have designed a clinical decision making aid in the form of a flow chart to help eye care practitioners to choose appropriate nutritional advice for their patients. The aim of this study is to validate this clinical decision making aid.

Why have I been chosen?

This study is open to any eye care practitioner (optometrist or ophthalmologist) in the UK who is currently practicing.

Do I have to take part?

No. Participation is entirely voluntary. If you decide to take part and later wish to withdraw, please note the study will close on 1st March 2015.

What will I have to do if I take part?

Firstly, there is a short survey to complete that takes approximately five minutes and will assess your feelings on giving nutritional advice to patients with, and at risk of, AMD. The survey will mainly involve answering questions on a scale of 0 -100. An example question is:

- "How confident are you in providing nutritional advice to patients with AMD?"

The survey is accessed online using a link that we will make available to you. Once this survey has been completed, you will be provided with a link to the clinical decision making aid that you can print out. We would like you to use the aid for two weeks, and then we will email you to ask you to complete a follow up survey that will take approximately five minutes again, and is very similar to the first survey.

What are the benefits of taking part?

The clinical decision making aid will be yours to keep. There will be a 'Frequently Asked Questions' leaflet accompanying it, that will provide you with information regarding current research in nutrition for AMD.

Are there any risks of disadvantages of taking part?

There is very little risk of disadvantages in taking part. Some practitioners may lack confidence in the area of nutrition for AMD, but participation is anonymous and their confidence has the potential to improve after using the clinical decision making aid.

What will happen to the results of the study?

The results are anonymous and will be used to validate the clinical decision making aid. The data is kept on a survey database that only the researchers have access to, and all other data is kept on one password protected computer in a locked room.

Who has reviewed the study?

The study has been reviewed by the School of Life and Health Sciences Ethics Committee, Aston University as well as members of the Aston University Ophthalmic Research Group.

Researchers

Rebekah Stevens

Optometrist, Clinical Demonstrator, PhD student. Vision Sciences department, Aston University. Contact: r.stevens3@aston.ac.uk

Hannah Bartlett

Optometrist. Senior Lecturer. Vision Sciences department, Aston University.

Contact: h.e.bartlett@aston.ac.uk

Richard Cooke

Psychologist. Senior Lecturer. Psychology department, Aston University.

Contact: r.cooke@aston.ac.uk

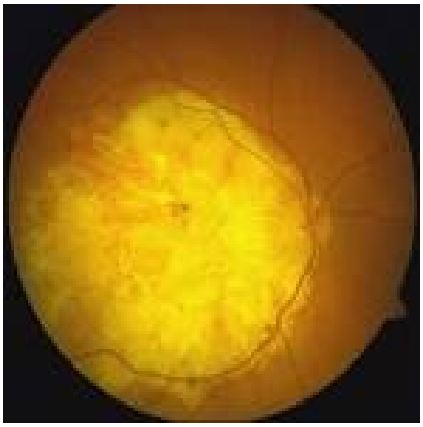
Where can I get more information?

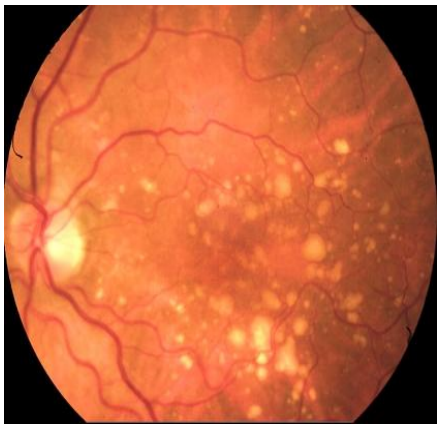
Please contact Rebekah Stevens (r.stevens3@aston.ac.uk) if you would like any more information about the study.

What if there is a problem?

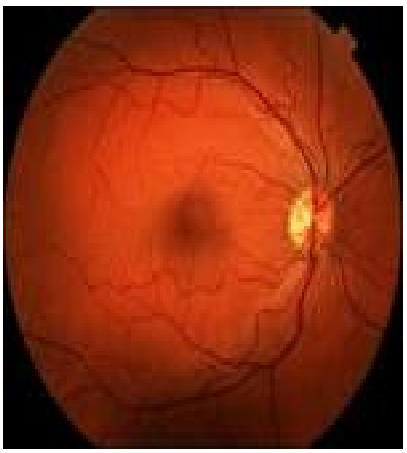
If you have any concerns about the way in which the study has been conducted, then you should contact the Secretary of the University Research Ethics Committee, Mr John Walter, at j.g.walter@aston.ac.uk or telephone 0121 204 4665

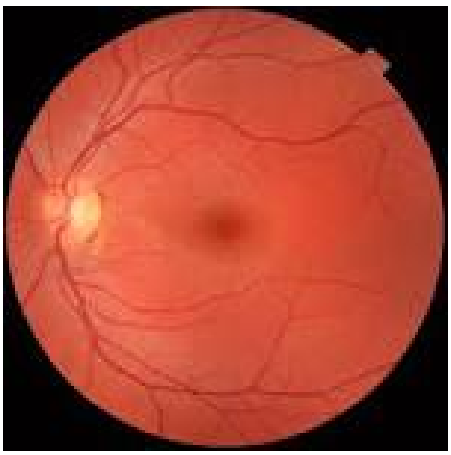
Appendix 13. Student clinical scenarios



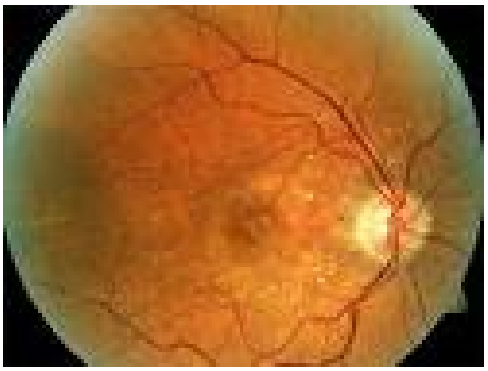
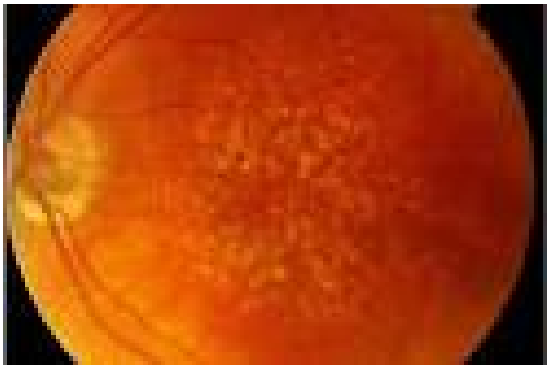


1) Large drusen in one eye, and geographic atrophy in fellow eye with male patient aged 78

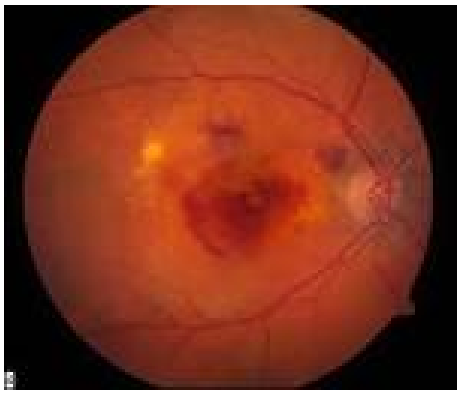
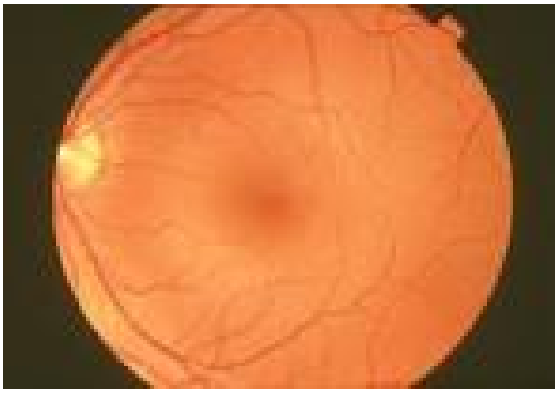




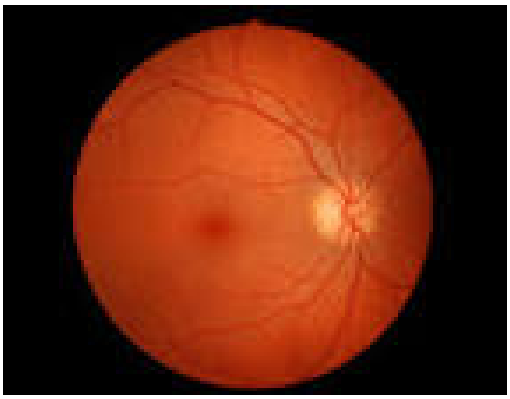
2) Normal healthy retinas of female aged 65, with family history of AMD.

3) Large drusen in one eye, and geographic atrophy in fellow eye with female patient aged 48

4) Large haemorrhage in one eye, and a normal fellow eye in female aged 80.




5) Small drusen in one eye, and a normal fellow eye in male aged 60

Appendix 14 – Optician article given to participants as AREDS 2 information.

Appendix 15 – Age-related macular degeneration patients' awareness of nutritional factors.

Appendix 16 – Dietary Analysis and nutritional behaviour in people with and without age-related macular disease