BMJ Open

How does age-related macular degeneration affect real-world visual ability and quality of life? A systematic review

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To cite: Taylor DJ, Hobby AE, Binns AM, *et al*. How does age-related macular degeneration affect real-world visual ability and quality of life? A systematic review. *BMJ Open* 2016;**6**:e011504. doi:10.1136/bmjopen-2016-011504

► Prepublication history and additional material is available. To view please visit the journal (http://dx.doi.org/10.1136/bmjopen-2016-011504).

Received 12 February 2016
Revised 21 September 2016
Accepted 4 November 2016

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ABSTRACT

Objectives: To review systematically the evidence of age-related macular degeneration (AMD) affecting real-world visual ability and quality of life (QoL). To explore trends in specific topics within this body of the literature.

Design: Systematic review.

Methods: A systematic literature search was carried out using MEDLINE, EMBASE, CINAHL, PsycINFO, PsychARTICLES and Health and Psychosocial Instruments for articles published up to January 2015 for studies including people diagnosed with AMD, assessing real-world visual ability or QoL as an outcome. Two researchers screened studies for eligibility. Details of eligible studies including study design, characteristics of study population and outcomes measured were recorded in a data extraction table. All included studies underwent quality appraisal using the Mixed Methods Appraisal Tool 2011 Version (MMAT).

Results: From 5284 studies, 123 were eligible for inclusion. A range of approaches were identified, including performance-based methods, quantitative and qualitative patient-reported outcome measures (PROMs). AMD negatively affects tasks including mobility, face recognition, perception of scenes, computer use, meal preparation, shopping, cleaning, watching TV, reading, driving and, in some cases, self-care. There is evidence for higher rates of depression among people with AMD than among community dwelling elderly. A number of adaptation strategies have been associated with AMD of varying duration. Much of the research fails to report the type of AMD studied (59% of included studies) or the duration of disease in participants (74%). Of those that do report type studied, the breakdown is as follows: wet AMD 20%, dry AMD 4% and both types 17%.

Conclusions: There are many publications highlighting the negative effects of AMD in various domains of life. Future research should focus on delivering some of this research knowledge into patient management and clinical trials and differentiating between the types of AMD.

Strengths and limitations of this study

- This is the first systematic review to include patient-reported and performance-based outcome measures in this field.
- The most recent systematic reviews in this field were published almost 10 years ago.
- Studies about the effect of age-related macular degeneration (AMD) on reading were not included as this is a topic that is already well reported on.
- A large proportion of included studies did not report type of AMD investigated or duration of AMD.

INTRODUCTION

Age-related macular degeneration (AMD) is a highly prevalent condition which causes loss of central vision.[1] It is the most common cause of blindness in developed countries and is labelled a 'priority eye disease' by the WHO.[2] In the UK, an incidence of 71 000 new cases of late AMD per year has been estimated.[3] Incidence and prevalence are set to rise as the population ages.[4]

AMD can be divided into early and late stages. The early stage, also referred to as age-related maculopathy (ARM), is characterised by yellow/white deposits (drusen) beneath the retinal pigment epithelium, and areas of hyperpigmentation or hypopigmentation.[5 6] Later stages may take one of two forms: neovascular (wet or exudative) AMD (nAMD), characterised by growth of new blood vessels beneath the retina with a tendency to leak, causing sudden vision loss, or geographic atrophy (GA, dry AMD), characterised by sharply demarcated areas of hypopigmentation in which choroidal blood vessels are more visible than in surrounding areas, causing more insidious vision loss.[5 7]

Quality of life (QoL) is a subjective measure[8 9] influenced by factors including expectations, relationships,[10] routine,[11] health and disability.[12] QoL is often used interchangeably with health status, functional status and health-related quality of life,[13 14] although there are subtle differences

between each of these[15] (see table 1). For the purpose of this article, we use QoL to encompass these slightly different terms.

QoL is often measured using patient-reported outcome measures (PROMs), normally via a questionnaire.[16 17] This allows 'a better understanding of the relationship between the pathophysiology of eye disease and patient-reported functioning'.[18] Performance-based measures are another type of tool for assessing functional ability or disability. Results from PROMs and performance-based measures may differ, but this review will consider both.[19–21]

As AMD incidence increases, it is important to understand how it affects visual function and QoL. Previous large-scale systematic reviews, the most recent published a decade ago,[22 23] concentrate on PROMs and do not describe real-world performance-based measures. More recent systematic reviews[24–28] are much smaller scale, concentrating on only one aspect of patients' experiences with AMD, and again, do not consider performance-based measures. Progress in this field could be an important step towards designing appropriate strategies for monitoring disease progression, rehabilitation, justification of new treatments and designing more meaningful outcomes for clinical trials.

This systematic review investigates the effect of AMD on visual disability and QoL and explores trends in specific topics within this body of literature.

METHODS

A search of the electronic databases MEDLINE, EMBASE, CINAHL, PsycINFO, PsychARTICLES and Health and Psychosocial Instruments was undertaken using keywords relating to AMD, QoL and real-world visual disability (see online supplementary appendix 1 for a detailed breakdown of search terms).

Retrospective and prospective reference list searches were conducted for studies meeting eligibility criteria and relevant reviews. Eligible studies involved people diagnosed with AMD, considered an aspect of real-world visual ability or QoL as an outcome, were available in English and involved human participants only. Studies were excluded if they only considered standard clinical measures of visual function. They were also excluded if outcomes were a result of an intervention or treatment (including clinical trials) or if an abstract only was published (conference proceedings). Review articles were excluded. Two authors (DJT and AEH) screened studies to assess eligibility. In the case of disagreements unresolved through discussion, a third author (DPC) was consulted. Owing to the extensive body of literature and existing reviews[29 30] concerning the impact of AMD on reading, studies concerning this were excluded.

Relevant information (including study design, study population characteristics and outcomes measured) from eligible papers was entered into a data extraction table.

Quality appraisal was conducted using the Mixed Methods Appraisal Tool 2011 Version (MMAT).[31] This is a recently developed but increasingly recognised tool, with over 90 citations in the literature, including a number of high-quality systematic reviews.[32–34] This tool was chosen for this study because it facilitates methodological appraisal of quantitative, qualitative and mixed methods studies. Scores are based on meeting criteria, which differ according to study type. For each criterion met, a score of 1 is given, up to a possible total of 4 for each study. Criteria which are not met, or those for which information is not given in the study, a score of 0 is given. Full details of grading criteria are shown in table 2.

RESULTS

The search was conducted on 6 January 2015 yielding 5712 results. An additional 15 studies were identified for inclusion from reference lists of relevant primary studies and reviews. Reviewers were in agreement for 5045/5269 (95.7%) of records. Discrepancies were resolved as described previously. A total of 123 studies were selected for inclusion. Online supplementary appendix 2 summarises the characteristics and outcomes of these studies. Many studies were excluded at the record screening stage. The main reasons for this were that they did not report outcomes relating to QoL or real-world visual ability or did not include participants with AMD. Details of assessment of articles for eligibility along with reasons for excluding full-text articles are shown in figure 1.

All 123 included studies underwent methodological quality appraisal using the Mixed Methods Appraisal

Table 1 Definitions of selected terms related to quality of life (adapted from Patrick *et al*[15])

Term	Definition
Functional status	An individual's effective ability to perform valued roles, tasks or activities (eg, going to work, playing sports or housework).
Health-related quality of life (HRQoL)	Personal health status. HRQoL usually refers to aspects of our lives that are dominated or significantly influenced by our mental or physical well-being.
Quality of life (QoL)	An evaluation of all aspects of our lives, including, for example, where we live, how we live and how we play, encompassing life factors such as family circumstances, finances, housing and job satisfaction.
Well-being	Subjective bodily and emotional states; how an individual feels; a state of mind distinct from functioning that pertains to behaviours and activities.

Table 2 MMAT grading criteria (adapted from Pace *et al*[31])

Types of mixed methods study components or primary studies	Methodological quality criteria
	(See tutorial for definitions and examples)
Screening questions (for all types)	Are there clear qualitative and quantitative research questions (or objectives), or a clear mixed methods question (or objective)? Do the collected data allow address the research question (objective)? Eg. Consider whether the follow-up period is long enough for the outcome to occur (for longitudinal studies or study components). *Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions*
1. Qualitative	1.1 Are the sources of qualitative data (archives/documents/informants/observations) relevant to address the research question (objective)? 1.2 Is the process for analysing qualitative data relevant to address the research question (objective)? 1.3 I appropriate consideration given to how findings relate to the context, eg the setting, in which the data were collected? 1.4 Is appropriate consideration given to how findings relate to researchers' influence, eg through their interactions with participants?
2. Quantitative randomised control (trials)	2.1 Is there a clear description of the randomisation (or an appropriate sequence generation)? 2.2 Is there a clear description of the allocation concealment (or blinding where applicable)? 2.3 Are there complete outcome data? 2.4 Is there low withdrawal/drop-out (below 20%)?
3. Quantitative non-randomised	3.1 Are participants (organisations) recruited in a way that minimises selection bias? 3.2 Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes? 3.3 In the groups being compared (exposed vs non-exposed; with intervention vs without; cases vs controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups? 3.4 Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?
4. Quantitative descriptive	4.1 Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)? 4.2 Is the sample representative of the population understudy? 4.3 Are measurements appropriate (clear origin, or validity known, or standard instrument)? 4.4 Is there an acceptable response rate (60% or above)?
5. Mixed methods	5.1 Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)? 5.2 Is the integration of qualitative and quantitative data (or results) relevant to address the research question (objective)? 5.3 Is appropriate consideration given to the limitations associated with this integration, eg the divergence of qualitative and quantitative data (or results) in a triangulation design? *Criteria for the qualitative component (1.1 to 1.4), and appropriate criteria for the quantitative component (2.1 to 2.4, or 3.1 to 3.4, or 4.1 to 4.4), must be also applied).*

MMAT, Mixed Methods Appraisal Tool.

Tool 2011 Version (MMAT).[31] Eleven studies (9%) had a score of 2, 33 (27%) scored 3 and the remaining 79 (64%) had a score of 4. Most frequent sources of bias were related to groups not being comparable and differences between groups not being accounted for, followed by issues regarding recruitment and sample size. Online supplementary appendix 3 shows details of quality appraisal for all included studies.

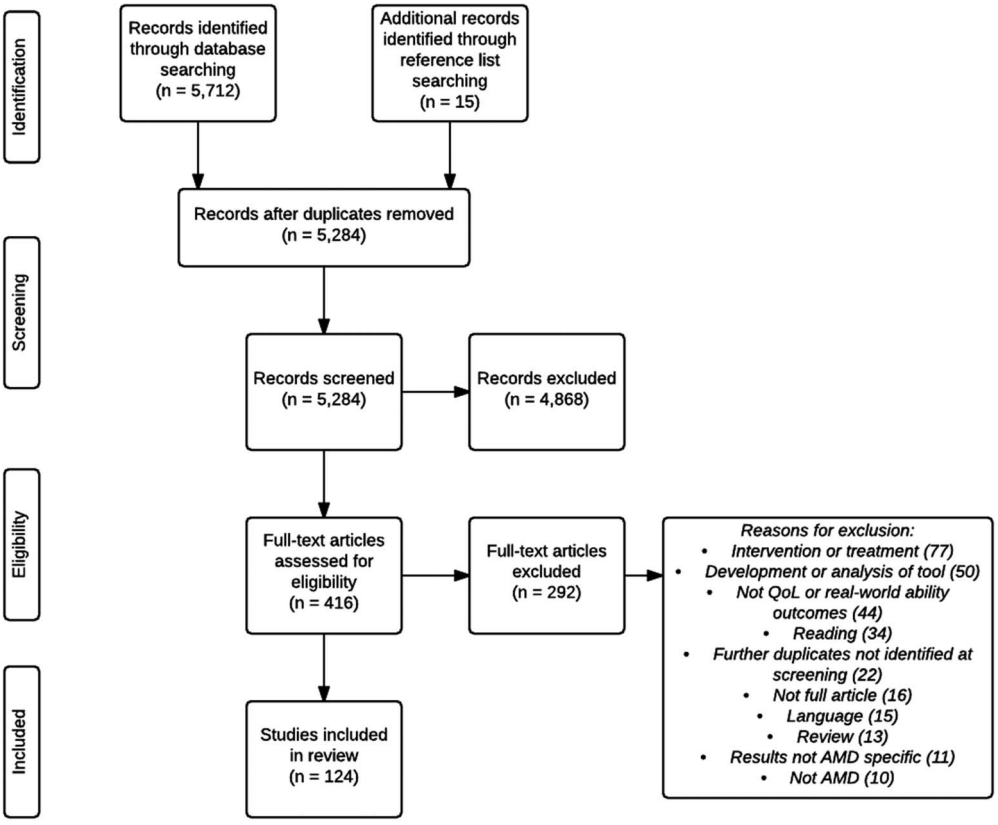

Figure 1 Study selection process.

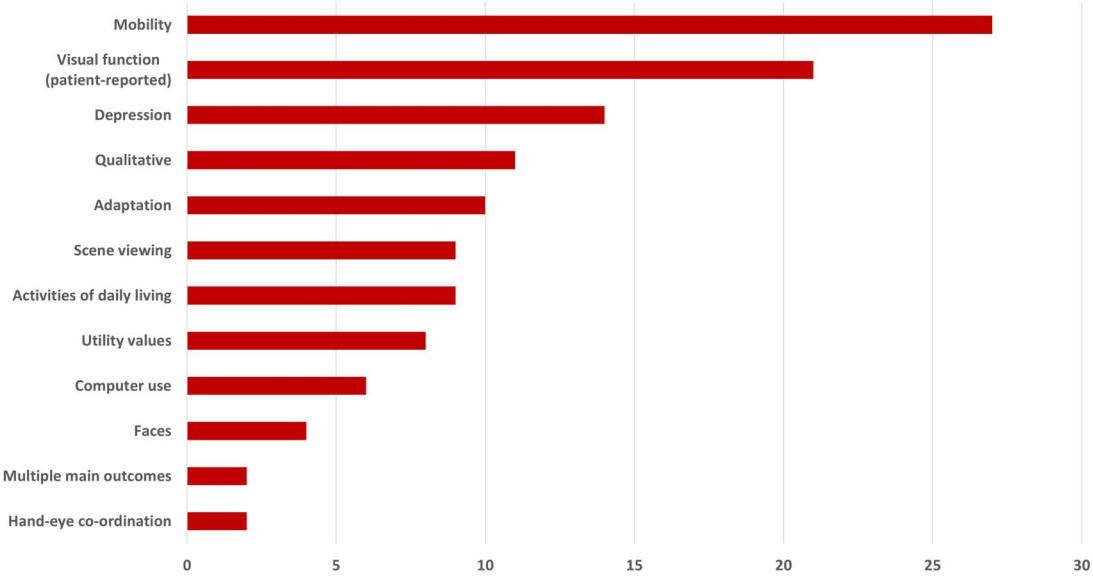

Figure 2 Domains of QoL and real-world visual ability covered by included studies.

Below is a short description of the main findings of studies included in the systematic review. For further details of the studies, including experimental design and sample sizes, see online supplementary appendix 2. The overview of the study findings is organised according to the outcome main dimension. Figure 2 shows the wide range of domains reported by studies included in this review, the most frequent of which are mobility (22% of studies) and patient-reported visual function (17%).

Performance-based studies

Mobility

Twenty-one studies, including 1131 people with AMD, investigating the effect of AMD on mobility performance were identified. The majority of these (n=14) were case–control studies, followed by cross-sectional studies (n=5), along with one cohort study and one longitudinal study.

Basic mobility

Individuals with AMD have been found to travel less and be less likely to drive than those with other eye diseases.[35] They are reported to have poorer balance and postural stability than non-AMD participants under a range of conditions.[36–38] Binocular central scotoma size was a predictor of mobility performance in an obstacle course for people with AMD.[39]

Road crossing

People with AMD were equally able to detect traffic gaps when crossing roads, but with a longer delay, reducing safety margins compared with fully sighted controls and those with peripheral vision loss.[40] People with AMD fixated primarily on vehicles rather than traffic lights while waiting to cross,[41] and they have been shown to make fewer head turns shortly before road crossing, preventing up-to-date road status information being gathered.[42] Overall, however, people with AMD were similar to age-related controls in accuracy and precision of their road crossing decisions.[43]

Travel patterns

A uniquely designed case–control study investigated travel patterns using a cellular tracking device.[44] Among 65 participants with AMD, average excursion distance and span of travel reduced with visual acuity (VA) loss.

Driving skills

One case–control study[45] compared detection of traffic signals in four small groups of volunteers: young and elderly visually healthy, ARM (n=8, with depressed VA, fundus changes such as drusen and pigmentary changes, some central field defects and colour vision defects) and preARM (n=10, defined as normal VA with macular drusen and/or pigment changes). ARM patients had slower reaction times. Interestingly, the preARM group had results outside the limits set by controls, implying that real-world tasks may be affected before clinically measured function. Another case–control study[46] showed 10 AMD patients to perform worse than controls on an interactive driving simulator and an on-road driving test.

Effect of lighting conditions

Six studies assessed mobility under different lighting conditions.[47–52] People with AMD walked slowly and cautiously during light and dark adaptation, while fully sighted people only behaved in this way during dark adaptation, indicating that those with healthy vision respond during dark adaptation as though their vision were impaired.[48] People with AMD walk more cautiously, make more gait modifications while walking on altered surfaces[47] and have difficulty stepping on low contrast targets in dim light and during dark adaptation.[49] AMD affects navigating paths under low lighting[51] and curb navigation particularly during dim lighting and dark adaptation.[50] AMD patients performed worse on an obstacle course in dim lighting compared to well-lit conditions.[52]

Falls and miscellaneous

Two cross-sectional studies found that individuals with AMD have greater falls risk than those without[53] and that fear of falling results in activity limitation.[54] One case–control study[55] used eye tracking and audio feedback while participants watched video simulations of walking through a building: AMD volunteers made more comments and more fixations than controls.

Faces

Five studies (four case–control and one cross-sectional) including 171 people with AMD, investigating the effect of AMD on viewing faces were identified.

These studies cover a range of outcomes including familiar face recognition, facial expression discrimination and eye movements while viewing an image of a face in people with AMD.[56–60] AMD patients performed better at detecting whether a face had an expression or not than on categorising the expression.[57] In one case–control study,[56] only 26% of a group of 100 AMD patients correctly identified the facial expression on all four photographs shown. Familiar face recognition and facial expression detection performance has been estimated to worsen with reduced luminance.[58] One study reported significant differences in eye movements made by nine people with AMD compared to nine controls.[59] Another indicated perceived disability in face recognition to not correlate with actual face recognition performance.[60]

Scene viewing

Nine studies investigating the effect of AMD on scene viewing were identified. These included a total of 176 participants with AMD. These were all case–control studies.

People with AMD are reported to recognise isolated objects better than objects in scenes, coloured images better than achromatic images,[61] recognise an object in a scene more easily when enhanced with a border[62] and when placed on a related compared to an unrelated background.[63] AMD has been shown to affect processing of high-spatial frequency scenes.[64] Moreover, images have been shown to be more recognisable for AMD patients at lower spatial frequency bandwidths if the background is darkened.[65] One study asking participants whether or not a real-world target was present in a scene at varying levels of contrast found task success to be strongly related to contrast level.[66]

People with AMD have been reported to categorise scenes as natural versus urban faster and more accurately than indoor versus outdoor, while no differences were found between these conditions for visually healthy people.[67] In another study, participants undertook a natural versus urban scene categorisation task in which images were randomly presented in one of five locations on the computer screen.[68] While controls performed better when the image was presented centrally compared with peripheral presentation, AMD patients performed worse at all locations than controls and did not perform better for central than peripheral presentations.

In another experiment,[69] participants were presented with a view of a scene (the prime view) and asked to change the viewpoint in a computer program representing the scene, until the viewpoint matched the prime view. Controls (n=13) and AMD patients (n=19) had bias towards 'middle views' of a scene; this was more pronounced in AMD patients. Authors hypothesised that disruption to central vision causes incorrect scene perception.

Computer use

Six studies investigating the effect of AMD on computer use were identified. These included a total of 57 participants with AMD. Four of these were case–control studies, while two were case series.

AMD may result in difficulty using computers.[70–75] Performance in a simple task involving identification of commonly used computer icons was significantly associated with worsening VA, contrast sensitivity (CS) and colour vision defects in 18 people with AMD.[73] Other studies found that performance could also be affected by features of the graphical user interface,[70 71 74 75] although all but one[73] of these studies investigated only six or less people with AMD. Patients with dry AMD have been shown to benefit from auditory and haptic feedback when performing computer-based tasks.[72]

Other tasks

In a case–control study of 100 people with AMD (92 with nAMD), 48% were able to tell the time from a bold-faced wall clock 1.5 m away, 70% correctly identified the colour of four handkerchiefs coloured red, blue, tan and grey, and 68% correctly identified four commonly used household products when presented with well-known brands of cereal, tomato ketchup, dish detergent and milk.[56] Differences between people with (n=10) and without (n=10) AMD have been reported in a case–control study investigating performance of reach-to-grasp tasks.[76] A further case–control study[77] reported that poor handwriting legibility in eight patients with scotoma caused by AMD may be a result of difficulty placing letters in the correct location due to inability to view the writing area.

Patient-reported outcomes

Patient-reported visual function

Twenty-two studies investigating the effect of AMD on patient-reported general visual function were identified. These included a total of 10 877 participants with AMD. Twenty of these were cross-sectional studies and two were cohort studies.

The National Eye Institute Vision Function Questionnaire (NEI-VFQ) is a widely used PROM in AMD.[23] Average scores are reported to be poorer in people with AMD compared to those without[16 78–84] and, unsurprisingly, worse in more severe disease.[16 83–85] Results from studies using different tools are mostly aligned with these findings.[86–90] A prospective longitudinal study investigating change in visual function in 671 women with AMD over a 5-year period found worse NEI-VFQ scores in those with late AMD at the beginning and end of the study compared to those progressing from early to late AMD.[91] Two large-scale cross-sectional studies investigating 2194 and 1052 people with AMD found no association[84] and weak association[92] with early AMD, respectively, although a smaller study (n=106) using a different PROM did find impaired visual function in those with mild AMD.[88] Best and worst eye VA were found to contribute independently to NEI-VFQ scores.[1 93] NEI-VFQ scores were worse in individuals with binocular compared to monocular visual loss from AMD,[94 95] although 54 patients with blindness in one eye reported greater emotional distress than 54 with binocular blindness, perhaps due to uncertainty regarding future disease progression.[96] Interestingly, patients with high response on a neuroticism scale reported worse visual function than those with average response, regardless of VA.[97]

Mobility

Seven studies investigating the effect of AMD on patient-reported mobility were identified. These included a total of 655 participants with AMD. Four of these were cross-sectional, two were cohort studies and one was a longitudinal study.

Two separate retrospective studies have reported lower rates of motor vehicle collision among people with AMD compared to matched controls.[46 98] These and other studies concluded that AMD patients self-regulate by changing driving habits, for example, avoiding driving at night, in unfamiliar areas or over long distances.[99 100]

Higher self-reported fall rates have been reported among AMD patients compared with those without.[78–80] Among AMD patients, reduced CS and VA have been associated with more self-reported falls (using diaries).[101] Older women with AMD have been reported to have almost twice the risk of injurious falls (self-reported) than those without.[102] AMD has been associated with fear of falling,[103] and another PROM-based cross-sectional study concluded that limited life space and activities due to fear of falling seem to mediate the relationship between eye disease and depression.[104]

Utility values

Eight cross-sectional studies investigating the effect of AMD on utility values were identified. These included a total of 1768 participants with AMD.

Utility values, a type of PROM, give quantitative expressions of preference for given health states[23] and can be assessed using different methods. For example, standard gamble ascertains risk people would be willing to take in order not to have a certain health condition and the time trade off hypothetically assesses life years sacrificed in order to avoid the condition. Scores are normally presented on a scale between 0 and 1; higher scores indicate better health or less willing to take risks to avoid a condition. Average values for AMD range from 0.60 to 0.81;[105–107] patients with worse vision loss from AMD score lower than those with mild loss.[105] A different utility value scale yielded mean preference values for nAMD patients of 0.62 to 0.64.[108] Utility values allow comparisons between different health conditions. Values for AMD are comparable with asymptomatic HIV (0.69), mild osteoarthritis of the hip (0.69), mild and moderate angina (0.88 and 0.83), mild and moderate myocardial infarction (0.91 and 0.80) and diabetes mellitus (0.88).[109] Values reported for other eye diseases include glaucoma (0.64 to 1.0) and diabetic retinopathy (0.59 to 0.94).[110] One cross-sectional study[111] compared utility values between AMD and diabetic retinopathy and found comparable values for equivalent levels of VA loss in each disease. Another cross-sectional study[112] found CS to be a good predictor of utility values in 209 AMD patients.

Utility values are often established from members of the public who are given descriptions of the health condition being assessed; these tend to yield higher values than those from people with AMD.[113] This is supported by results of other studies[114 115] using time trade off scores which showed utility values were consistently overestimated by the public, non-ophthalmic and even ophthalmologists when compared to ratings by AMD patients themselves.[114 115] It may be impossible to appreciate the consequences of vision loss without having experienced them.[114]

Depression

Fourteen studies investigating the effect of AMD on depression were identified. These included a total of 1880 participants with AMD. Eight of these were cross-sectional, two were cohort studies, one was longitudinal and one was a case report.

Associations between levels of depression and AMD have been reported in the literature.[104] Estimated prevalence rates for depression range from 11% to 44% among AMD patients,[116–119] the highest of these figures is two to three times the rate found for elderly controls. In contrast, one cross-sectional study[120] found no association between AMD and depression. Differences between results may arise from different tools used to assess depression in these studies and different recruitment methods (clinic-based vs population/community-based sample). Selective mortality and limiting eligibility criteria have also been suggested as reasons for not finding an association in some studies.[120] Depression in AMD has been reported to be strongly correlated with increasing VA loss[121] and is predicted by neurotic personality.[122] In other studies depressive symptoms, even if minimal, were associated with loss of visual function regardless of VA level.[122–127] AMD patients (n=144) who reported poor adaptation to vision loss, especially with respect to acceptance of and compensation for vision loss, reported more depressive symptoms than those who adapted better.[128] One case report highlights risk of suicide because of AMD-related vision loss;[129] eye-care providers should be trained to identify patients at risk of suicidality.

Adaptation

Fourteen studies investigating adaptation to AMD were identified. These included a total of 1122 participants with AMD. Two of these were case–control, one was a cohort study, four were longitudinal and three were cross-sectional.

Studies have investigated adaptation to AMD based on Heckhausen and Schulz life-span theory of control.[130 131] Usage of internal resources (such as time and effort) was positively associated with ability to carry out activities of daily living, and external resource finding (such as using low vision services and aids) and increase of motivational commitment were positively associated with positive emotion.[131 132] External resource finding increased shortly after diagnosis, perhaps as patients initially sought advice and support.[133] Internal resource usage and motivational input have been found to decrease over time in AMD patients, while external resource finding and replacement of desired goals partially increased over this time.[134] External resource finding[135] and replacement of desired goals[133] increased as patients lost ability to carry out activities of daily living. Variations in coping strategies, along with cognitive ability, have been reported to influence self-report of visual function.[136]

One longitudinal study[137] found decline in positive mood over the first 2 years following diagnosis, followed by an increase between the third and fifth years, with some subsequent stability. AMD patients were found to have poorer life satisfaction, greater stress,[138] more emotional problems, greater social dysfunction[139] and impaired activities of daily living over a 5-year period[140] than those without.

Activities of daily living

Nine studies investigating the effect of AMD on activities of daily living were identified. These included a total of 1279 participants with AMD. Seven of these were cross-sectional, one was a case series and one was a case report.

Studies[21 141] report that 39–45% of AMD patients require help with at least one activity of daily living. These studies and others[78–80] suggest that between twice and eight times as many AMD patients require assistance with activities of daily living compared with those without. Severity of AMD is associated with these difficulties,[18] which are unlikely to be experienced if visual function is unaffected,[142] although night driving difficulties related to impaired scotopic sensitivity may occur while VA remains relatively good.[143] Activities commonly affected include meal preparation, travelling, cleaning, grooming, shopping, going out, navigating steps and pavement curbs, noticing objects, hobbies, watching TV, reading, driving (especially night driving) and using low vision devices.[18 21 88 143–145] In addition, ability to carry out activities requiring visual resolution, such as reading, can distinguish those who are capable of self-care only with those who are able to care for themselves and others. Likewise, ability to carry out household chores, such as preparing food, can distinguish those who are capable of self-care and those who are not.[146]

A case study[147] of a patient with bilateral ring scotomas from AMD reported difficulties in 'several activities of daily living', in particular driving and following the ball when playing golf. The patient was reported to find compensatory scanning eye movements a useful way of keeping desired areas in focus.

Qualitative data collection methods

Eleven studies using interviews, focus groups and diaries to assess how AMD affects visual disability or QoL were identified.[148–158] Their aims included illustrating 'living with AMD' and elucidating challenges caused by the condition.[148–155] Others investigated factors associated with successful adaptation to AMD.[156–158] The detailed results of these studies will be the subject of a subsequent report.

Trends

Our systematic review discovered that the literature representing the effects of AMD on QoL can be split into four categories: wet AMD only; dry AMD only; both types investigated with a breakdown and both types investigated but without a breakdown or type not reported. We show that the number of QoL and visual ability papers published in these categories is increasing over time in figure 3 (before 1985 no studies had been published on the subject). This increase may simply be attributed to the increasing number of papers and journals published. Nevertheless, these studies make up a minute proportion of the body of literature on AMD as a whole; a PubMed search for articles with 'age-related macular degeneration' in their title published between 2010 and 2014 yields 2458 results, while only 47 papers (<2%) published in this time were included in this systematic review.

DISCUSSION

Our review is timely. Although smaller scale systematic reviews have been published in this field,[24–28] the most recent large-scale systematic reviews were published about 10 years ago.[22 23] A more recent, non-systematic review published in 2013[159] cited only 30 papers. Over half of the papers included in our study were published since these other large-scale systematic reviews were conducted.

Poku *et al*[24] systematically reviewed utility values in patients with diabetic retinopathy, diabetic macular oedema and AMD in 2013 and concluded that according to the existing literature, AMD and diabetic retinopathy impact negatively on QoL, with most current research categorising by VA in patients' better-seeing eye. Tosh *et al*[25] also conducted a systematic review of preference-based measures of QoL in visual disorders in 2012 with similar results. Pinquart *et al*[26] conducted a meta-analysis comparing psychological well-being in people with and without visual impairment. Results suggest that psychological well-being may be affected by having visual impairment, and in particular that those with AMD are more at risk for reduced psychological well-being than those with other causes of visual

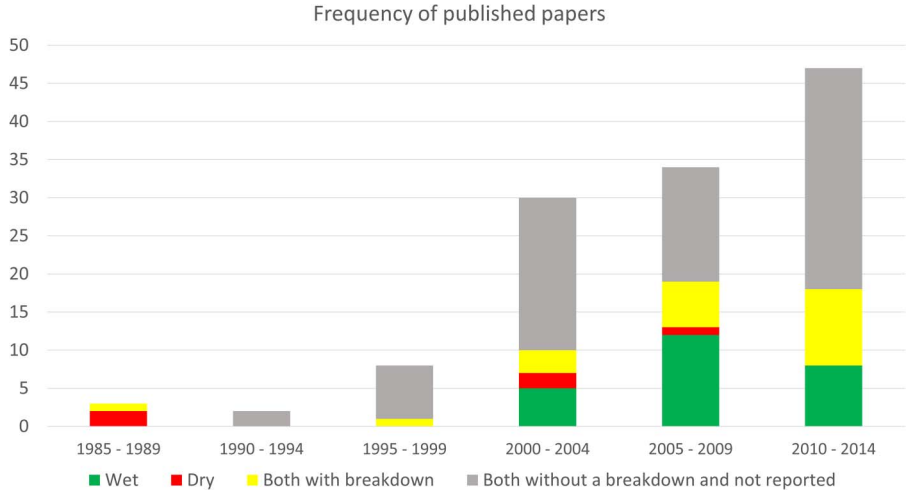

Figure 3 Frequency of published papers over time grouped by AMD type reported. AMD, age-related macular degeneration.

impairment. Depression and anxiety among those with AMD was systematically reviewed by Dawson *et al*[27] in 2014. Depression was found to be more prevalent among those with AMD than those without. Furthermore, worse disease severity was associated with increased depressive symptoms. However, similar to the results of this systematic review, wide variability was found, perhaps due to differences in sample size and tools used in included studies. Their results suggest no relationship between AMD and anxiety. Qualitative studies concerned with the experience of AMD were systematically reviewed in 2012.[28] Emerging themes centred on functional limitations, adaptation and independence, feelings about the future, interaction with health services, social engagement, disclosure and emotional impacts.

Our review is the first to integrate PROMs and performance-based studies assessing QoL and everyday visual function in AMD. The evidence presented in this study supports previous reviews' conclusions that AMD impacts negatively on people's lives. More is now understood about some of these areas of impact, for example, the relationship between AMD and falls,[53 54 78–80 101–104] and scene perception.[61–69] AMD negatively affects tasks including mobility, face recognition, perception of scenes, computer use, meal preparation, shopping, cleaning, watching TV, reading, driving and, in some cases, self-care. A large number of studies have highlighted the difficulties people with AMD may have with mobility, particularly in dim lighting.[48–51] Large-scale studies have reported invariably that many people with AMD self-report poor visual function; this worsens with AMD severity.[16 81 83 84 86 87 90–93 95 97] There is limited evidence surrounding the issues people with AMD may have with using computers, due to the small sample sizes of the majority of studies identified.[70–72 75]

A number of domains within people's lives are affected by AMD: social, emotional and physical. Our systematic review highlights the need for eye-care providers to be aware of this research evidence, and to be able to manage these patients, whether it be referral for low vision rehabilitation or help from social or counselling services. Previous research[114 115] has shown that people without AMD, including eye-care providers, consistently underestimate the effect of the condition and it would be interesting to discover whether public perceptions are different now, with the advent of newsworthy potential new treatments. For example, a Google search for news articles about 'age-related macular degeneration treatment' published in 2004 generates three web pages of results, while a search for articles on the same topic published in 2014 generates 76 web pages.

We have also identified interesting trends in the publication of studies in this field (figure 3). There were no publications on QoL and visual disability in nAMD before 2000, and then there was a sudden increase; this is noteworthy and may be explained by the development of new treatments for nAMD around this time.[160 161] These are likely to have resulted in increased interest in investigating QoL and functional impacts in order to assess clinical and cost-effectiveness outcomes of these new treatments.[106] Few papers report the type of AMD investigated (41%, n=51)—worrying given the functional differences between the disease types, along with their differing time courses and treatments.[27] It is, however, encouraging that more papers that include both types are now providing a breakdown between the two. Five and 25 papers focus solely on dry AMD and wet AMD respectively. This is disproportionate, given that dry AMD comprises ~90% of diagnosed AMD cases.[162] In addition, 74% of included studies (n=93) do not report disease duration. As psychological and functional effects can change over the time course of the disease, this should be an important feature on which to report and comment.

Our results are supported by other studies,[27 28] which discuss the lack of discrimination between wet and dry AMD in research. We spotlight this observation to be true in the majority of papers published in this field (figure 3). Critically, results from studies that did discriminate between the two indicate that QoL and visual function are affected in unique ways depending on disease type. For example, one study[126] reported more nAMD patients than dry AMD patients suffering from depression. Another[148] discussed the optimism that nAMD patients may feel receiving treatment and emphasised the sense of loss that those with dry AMD may suffer from due to lack of treatment. We think these findings are interesting, and more research addressing these differences is likely required.[28]

This study has limitations. First, only papers published in peer-reviewed journals were included. This is likely to have influenced the results found due to submission bias and/or publication bias. Second, the nature of this review meant that randomised control trials were excluded. Third, due to lack of translation resources, non-English language papers were excluded. Fourth, the impact of AMD on reading was not considered in this study because we felt this is a topic that is already very well reported on. For example, previous extensive reviews report reduced reading performance in AMD[29 30] and subsequently reading is one of the most common valued activities to be lost as a result of AMD.[23] It is also worth noting that research in this field is not straightforward. For example, disentangling the effects of age alone from age-related eye disease is a challenge that often requires well-defined age-matched or age-related controls. Moreover, isolating the effect of AMD when elderly people have comorbidities is also a challenge. Still, using MMAT for our appraisal revealed most studies to have high levels of methodological quality.

CONCLUSIONS

Performance-based measures and PROMs have shown AMD to negatively affect QoL and visual disability; it

affects many activities of daily living including, for example, mobility, driving, face recognition, scene perception and computer use. From earlier reviews, we know AMD also impacts critically on reading. Emotional impact can be severe. These impacts can differ over the time course of the disease, perhaps due to adaptation, and this should be acknowledged and investigated in future research. Future research in this field should also focus on delivering some of this research knowledge into the assessment of patients in clinical management and clinical trials. In other words, successful clinical management of AMD should not simply be about changes on a letter chart (eg, VA or CS) but must equate to correct decisions about intensifying treatment when patients are at risk of developing 'visual disability'. Furthermore, our review highlights a requirement to differentiate between types of AMD, especially as new disease-type specific treatments emerge for them.

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Contributors All the authors contributed to study design. DJT and AEH screened abstracts and full-text articles for inclusion. DJT appraised study quality. Any disagreements or uncertainties during the screening and quality appraisal process were referred to DPC. DJT drafted the manuscript, which was reviewed, edited and approved by DPC and AMB.

Funding This work was supported by an unrestricted investigator initiated research grant from Roche Products, UK.

Competing interests None declared.

Patient consent No.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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