# Searching for Objects in Everyday Scenes: Measuring Performance in People With Dry Age-Related Macular Degeneration

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**Purpose.** Treatment success in clinical trials for AMD would ideally be aligned to measurable performance in visual tasks rather than imperceptible changes on clinical charts. We test the hypothesis that patients with dry AMD perform worse than visually healthy peers on computer-based surrogates of "real-world" visual search tasks.

**Methods.** A prospective case-control study was conducted in which patients with dry AMD performed a computer-based "real-world" visual search task. Participants searched for targets within images of everyday scenes while eye movements were recorded. Average search times across the images were recorded as a primary outcome measure. Comparisons were made against a 90% normative limit established in peers with healthy vision (controls). Eye movement parameters were examined as a secondary outcome measure.

**Results.** Thirty-one patients and 33 controls with median (interquartile range) age of 75 (70–79) and 71 (66–75) years and logMAR binocular visual acuity 0.2 (0.18–0.31) and −0.06 (−0.12 to 0), respectively, were examined. Four, 18, and 9 patients were categorized as having early, intermediate, and late AMD, respectively. Nineteen (61%) patients exceeded the 90% normative limits for average search time; this was statistically significant (Fisher's exact test, $P < 0.0001$). On average, patients made smaller saccades than controls ($P < 0.001$).

**Conclusions.** People with dry AMD, certainly those with advanced disease, are likely to have measurable difficulties beyond those observed in visually healthy peers on "real-world" search tasks. Further work might establish this type of task as a useful outcome measure for clinical trials.

Keywords: age-related macular degeneration, geographic atrophy, search, visual search

Age-related macular degeneration (AMD) is the most common cause of vision impairment in the developed world.[1,2] The vast majority of people diagnosed with AMD have the "dry" form of the disease (early and intermediate AMD, and late AMD [geographic atrophy, GA]), for which there is no available treatment to arrest progressive loss of vision. Promisingly, however, there are several potential therapies currently reaching the stage of phase III randomized clinical trials (RCTs).[3] So how should we be measuring treatment success in these trials? Inevitably they need to be powered for functional outcomes approved by the Food and Drug Administration. However, changes in traditional clinical measures, such as visual acuity (VA), may not best reflect visual function in GA, because if atrophy does not involve the fovea, VA may remain relatively good, whereas visual function declines. Likewise, once the fovea becomes atrophic, VA may remain stable, whereas visual function continues to decline due to enlargement of atrophy.[4,5] Importantly, imperceptible changes on a clinical chart might not matter to the patient. So, perhaps clinical measurements should be supported by secondary outcomes that more directly relate to the patient. Asking people is one way to ascertain feelings about changes in visual function, and some RCTs for neovascular AMD have used patient-reported outcome measures.[6,7] Yet discrepancies have been shown between self-reported performance of everyday visual tasks and actual performance of the task[8,9] (Pardhan S, et al. *IOVS* 2016;57:ARVO E-Abstract 1974). A supplementary method would be to measure performance in surrogates of real-world visual tasks people encounter every day; an example of this idea is explored in this study.

Visual search is an important everyday task of looking for something in a cluttered visual environment. Interestingly, visual search in people with vision impairment has been shown to be a predictor for difficulties with mobility and performance of other daily activities.[10] Patients with AMD certainly self-report difficulties in searching and finding things.[11,12]

An ideal surrogate of visual search performance that directly relates to patients' day-to-day life should mimic the way in which people might search for things in the "real world." This could be, for example, finding an item on a supermarket shelf, the exit sign at a bus station, or an item of interest on a map. However, most visual search research in patient-based studies has been limited to using optotypes like searching for a letter "T" among distractors in the form of the letter "L."[10,13–15] Other studies concerning visual search performance on people with AMD-type visual function defects seemed to be confined to simulated scotomas in people who are otherwise visually healthy.[16–20] These allow for more controlled experimental design, yet simulated scotomas will never be entirely realistic[21,22]; self-reported perception of scotoma has been reported

to vary enormously between patients.[23] In addition, there is a reported disconnect between visual search performance using arrays of optotypes and search in "real-world" scenes among people with eye disease.[24,25]

When searching for targets, the eyes move in patterns of saccades (movements of the eyes from one point to the next) and fixations (during which the eyes are stable, directing their gaze to a certain point). These eye movements have been shown to be affected in non–"real-world" types of visual search tasks in AMD.[16,26] More recently, eye movements during a "real-world" visual exploration task have been reported to be different in patients with neovascular AMD compared with visually healthy peers.[27]

This study, therefore, investigated the primary hypothesis that people with dry AMD perform worse than visually healthy peers on a computer-based surrogate of "real-world" search tasks in a prospective case-control study. A secondary aim investigates whether eye movements during the tasks differ in people with dry AMD compared with those without.

## Methods

### Study Participants

People with dry AMD were recruited from Moorfields Eye Hospital Trust London, optometrists local to the university, and the membership of the Macular Society (https://www.macularsociety.org/, available in the public domain). Patients were required to be 60 years or older, have sufficiently clear ocular media, have adequate pupillary dilation and fixation to allow quality fundus imaging, and to have dry AMD (early/intermediate/late) in their better-seeing eye (assessed by VA). Fellow eyes of patients were permitted to be of any AMD status. Visual acuity was required to be logMAR 0.7 or better (Snellen equivalent of 6/30). Patients were excluded if they had neovascular AMD in their better-seeing eye, had any ocular or systemic diseases that could affect visual function or history of medication known to affect visual function (e.g., tamoxifen or chloroquine), or high risk of angle closure during pupillary dilation (Van Herick $<$ Grade 2, history of angle closure or experience of prodromal symptoms of angle closure). In addition, patients were required to pass an abridged version of the Mini Mental State Evaluation[28] and to have sufficient knowledge of the English language to carry out a semi-structured interview with the study investigator.

Visually healthy controls were recruited from the City Sight Optometry Clinic at City, University of London. People attending this clinic for eye examinations are invited to sign up to be contacted if they wish to be recruited for research studies for which they might be a potentially suitable participant. Eligibility criteria for controls was the same as for AMD patients, except participants were required to have no AMD (or any other eye disease) in either eye, and monocular VA of logMAR 0.3 (6/12) or better.

The study was approved by a National Health Service Research Ethics Committee and was conducted according to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant before examination. Participant information was anonymized before being entered into a secure computer database.

### Clinical Examination and Screening

After providing informed consent, participants underwent a series of baseline examinations to evaluate their AMD status and to ensure eligibility for participation. These tests were conducted by an optometrist (DJT). Structured history and symptoms were taken, including questions from the EuroQol-5D questionnaire.[29] Best-corrected VA was tested using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, and contrast sensitivity (CS) with the Pelli-Robson chart. Van Herick technique was used to assess the anterior chamber angle.

Following the study tests, participants underwent dilated fundus examination. Lens clarity was graded using the slit lamp biomicroscope, according to the Lens Opacities Classification System III grading scale.[30] Fundus imaging was conducted, including color fundus photography, spectral-domain optical coherence tomography, and fundus autofluorescence. These were used to classify and grade AMD status by the better eye as early, intermediate, or late according to the Beckman classification scale.[31] This widely used scale grades macular disease according to drusen size, pigmentary abnormalities, and presence/absence of GA or neovascular AMD.

### Experimental Procedure

This study procedure replicates one described elsewhere.[32] Participants were seated at a chin rest 60 cm from a 56-cm cathode ray tube computer monitor displaying at a resolution of 1600 $\times$ 1200 at a refresh rate of 100 Hz (Iiyama Vision Master PRO 514; Iiyama Corporation, Tokyo, Japan). Trial frames with optimal refractive correction established during baseline testing were worn by all participants so that any obstructions to the field of view caused by spectacle frames would be equivalent for all participants. Participants were tested binocularly.

Eye movements were recorded using the Eyelink II system (SR Research Ltd., Ottawa, Ontario, Canada). Pupil position was sampled monocularly (the chosen eye was alternated between participants). Participants rested their heads against a chin rest and a forehead bar to minimize head movements; the Eyelink II's head movement detection system compensated for any head movements that did occur by adjusting the point of regard accordingly. The Eyelink II's proprietary algorithm was used to calibrate and verify the subject's point of regard in response to prompts shown at different locations of the screen before starting the task, and before each individual trial drift correction was performed. When a large drift was detected, recalibration was performed.

In each trial, participants were instructed to search for a target item within a digital photograph of an everyday indoor or outdoor scene presented on the computer screen. Examples of photographs used in the study are shown in Figure 1. These were 40.8 cm (width) $\times$ 30.6 cm (height) subtending a half-angle of 20.3° $\times$ 14.9°. Images were chosen to represent a range of visual search tasks that people may need to perform in their day-to-day lives. Before each image was shown, instructions were displayed on the computer screen, and the operator read these instructions out loud simultaneously. A central target was then shown on a gray background and the trial would not start until the Eyelink II had detected the participant's gaze was directed at the target. This ensured that all participants were looking at the same place when the trial started. Three practice images were displayed first, followed by 15 test images. The 15 test images were presented in a random order. Participants were instructed to indicate verbally once the target item in the image was detected. This was verified by the same experimenter (DJT) by ensuring that their gaze, as recorded by the Eyelink II was directed to the target. Search durations for each image were recorded; all search durations longer than 60 seconds were censored at this value.

The primary outcome measure for this experiment was the median search duration calculated across the 15 trials for each person. Recorded eye movement parameters, directly taken


Figure 1. Examples of photographs used in this experiment. In (**a**), participants were asked to find the name of the street, and in (**b**), participants were asked to find the castle. (Images were displayed at a higher resolution than shown here.)

from Eyelink II, were considered to be secondary outcome measures. For each participant, a median value was calculated across the 15 trials to estimate average saccades per second, average saccadic amplitude, and average fixation duration.

## Data Analysis

A 90% normative reference limit was generated from the distribution of ranked median search times recorded in the visually healthy controls. This limit was estimated by a direct percentile method because the data were skewed.[33] Median search times for AMD participants were then specifically compared with this limit and comparisons between the AMD groups were investigated. A similar analysis was carried out for each of the three eye movement parameters. Univariate associations between median search time and VA, CS, and age were explored. Statistical analysis was carried out using SPSS Statistics 22 (IBM Corp., Somers, NY, USA).

## Results

Thirty-one people with AMD (84% female) with a median (interquartile range [IQR]) age of 75 (70–79) years and 33 visually healthy controls (55% female) with a median (IQR) age of 71 (66–75) years were eligible for this study; patients were

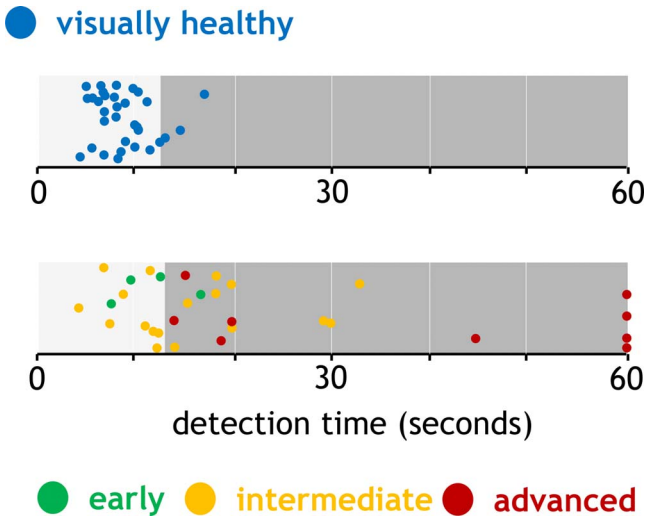


Figure 2. Median search durations for participants across images stratified by AMD group. The 90% normative limits set by controls are illustrated by the darker shaded area on the right of both graphs. (Some vertical jitter is added to the plotted points.)

slightly older on average than controls (Mann-Whitney $U$ test, $P = 0.01$). Median (IQR) duration of AMD was 4 (2–5) years. Participants had reasonable general health (ascertained by structured history and symptoms). Median (IQR) ETDRS corrected binocular logMAR VA was 0.20 (0.18–0.31) and –0.06 (0.12–0) in the patients and controls, respectively. The difference between these values was statistically significant (Mann-Whitney $U$ test, $P < 0.001$). Median (IQR) Pelli-Robson CS values were 1.65 (1.43–1.95) and 1.95 (1.95–1.95) in patients and controls, respectively. The difference between these values was statistically significant (Mann-Whitney $U$ test, $P < 0.001$).

When stratified by the Beckman classification,[31] according to better eye, 4, 18, and 9 patients were classified as having early, intermediate, and late (GA) AMD, respectively. Median (range) ETDRS corrected binocular logMAR VA for the people with no AMD, and early, intermediate, and late AMD was –0.06 (–0.22 to 0.08), 0.2 (0.18–0.28), 0.19 (0.02–0.44), and 0.38 (0.20–0.58), respectively.

Median (IQR) search durations for AMD patients and controls were 15.3 (11.7–24.3) and 8.3 (6.9–10.3) seconds, respectively. Nineteen (61%) patients, including all of those with late AMD, exceeded the 90% normative limits for delayed average search time set by the visually healthy controls (Fig. 2), and this was statistically significant (Fisher's exact test, $P < 0.001$). Individual graphs showing search durations for each individual image are available in Supplementary File S1.

There was no statistically significant association between age and average search time in the controls (Pearson's correlation coefficient [$r$] = 0.08, $P = 0.65$) or the AMD patients ($r = 0.21$, $P = 0.25$). There was a hint of positive association between AMD duration and average search time but this was not statistically significant ($r = 0.34$, $P = 0.08$). Among AMD patients there were significant associations between average search time and VA ($r = 0.72$, $P < 0.001$), and CS ($r = –0.82$, $P < 0.001$).

When trials were organized by "type," there were no statistical differences between search durations for outdoor images ($n = 9$) compared with indoor images ($n = 6$) (Mann-Whitney $U$ test, $P = 0.33$). Likewise, no statistical differences were found between search durations for search tasks involving reading text (e.g., "what is the price of the yellow

Table. Eye Movement Parameters Expressed as Median (IQR)

| Eye Movement Parameter | AMD Group, $n = 31$ | Control Group, $n = 33$ | $P$ Value |
|---|---|---|---|
| Fixation durations, ms | 288.1 (267.2–320.7) | 291.9 (268.9–312.6) | 0.88 |
| Saccadic amplitude, degrees | 4.1 (3.8–4.5) | 4.89 (4.5–5.2) | $< 0.001$ |
| Saccades per second | 2.9 (2.6–3.1) | 2.8 (2.6–3.0) | 0.45 |

smoothie drink?" "please find and read out loud the street name") and those that did not (e.g., "please find the hanging basket," "how many bins are there?") (Mann-Whitney $U$ test, $P = 0.45$).

The secondary outcome measures for this study were eye movement parameters (see Table). A video showing an example of eye movements recorded for all participants during one task is shown in Supplementary File S2. We found no differences between groups in fixation duration or saccades per second. Yet the people with AMD tended to make smaller saccades than controls and this was statistically significant.

Because of the difficulties some people with AMD have in foveating the target during calibration of the eyetracker, some patients were able to achieve "GOOD" calibration, but only "FAIR" or "POOR" validation during the calibration phase of the eye tracker. This is an issue that has been noted previously in people with AMD.[14] As a result of this, we can assume eye-tracking accuracy for patients was poorer for patients than controls. When the eye movement analysis was repeated purely for those who achieved GOOD calibration and validation ($n = 16$) compared with the 33 controls, saccadic amplitude remained significantly smaller for those with AMD than for those without ($P < 0.001$), there was no difference in fixation duration between AMD patients and controls ($P = 0.19$), and AMD patients made fewer saccades per second than those without, although the statistical significance was weak ($P = 0.04$).

Search durations and eye movement parameters did not differ significantly between males and females (Mann-Whitney $U$ test, search durations $P = 0.16$, fixation durations $P = 0.29$, saccadic amplitude $P = 0.22$, saccades per second $P = 0.22$).

## Discussion

Visual search is an important everyday task. Performance in a visual search task has also been shown to be a predictor of problems with mobility and other daily activities.[34] Existing research has focussed on arrays of optotypes or examining volunteers given simulated scotomas rather than participants with ocular pathology. Other studies using real-world–type tasks do not differentiate between type of age-related vision loss.[35] We used visual search tasks based on everyday scenarios and participants with actual scotomas. Median search durations were, perhaps unsurprisingly, worse for patients than for controls. The experimental effect was large: average search durations for participants were almost twice those for controls. Many of the people with AMD, including all those classified with GA in their better eye, fell outside a "normal" limit for the task. Average VA in the AMD group, although reduced, fell within the UK's legal requirements for driving, and this was noteworthy. This result agrees with previous research that people with AMD take longer to find targets in a visual search task than people without scotomas. Our study adds to this knowledge because we considered a group of people specifically with dry AMD and we used realistic surrogates of an "everyday" search task; this is likely more applicable to the real world than searching for optotypes in an array of distractors. In particular, our results highlight the burden of a diagnosis of GA with this type of everyday task as well as showing that some people with less severe vision impairment (intermediate AMD) may have more difficulties with these sorts of activities than previously believed.

A number of theories attempt to explain extended search duration in those with central scotomas. It may occur as a result of the need for increased fixation durations.[19,36] Yet increased fixation duration is not consistently reported across studies investigating visual search in people with central scotomas, and our study did not find a significant difference in fixation durations between AMD patients and controls. Others[27,37] discuss the increased number of saccades that may be required to attempt to bring a target of interest onto an area of healthy retina. Our results support this idea in part; the visually healthy participants in our study made more saccades per second on average than the patients during their search duration but this was only really apparent after we filtered the data by the quality of the calibration of the eye-tracking experiments.

Bertera[20] reported search durations for participants with an artificial central scotoma to double in comparison with "no-scotoma" conditions for difficult search tasks. They found no difference in search times between scotoma and no-scotoma conditions for easier search tasks. In our study, the largest proportional increase in median search durations occurred for search tasks involving finding and reading street signs, increasing search durations by 5-fold and 8-fold (see Supplementary File S1).

Cornelissen et al.[16] found larger saccadic amplitudes among participants with central scotoma; conversely others report no difference between those with and without central scotomas.[19,20] Crucially, these experiments were conducted using artificial scotomas, rather than people with actual vision loss. In our study, saccadic amplitudes were smaller on average among participants with AMD than those without; this aligns with results from a visual search study on central scotomas in people with Stargardt's disease.[26] Smaller saccadic amplitudes also have been observed during reading for people with AMD.[38] It has been suggested[32] that people with scotomas may make smaller eye movements to avoid their visual target falling into the scotoma.

There are limitations to this study. Although the tests were designed as surrogates of real-world tasks, performing a task at a computer screen and performing the same task in everyday life are not the same. However, we believe that this test has much better real-world applicability than search tasks conducted using arrays of optotypes. In addition, although participants were screened for cognitive defects and underwent structured history and symptoms questioning to ascertain reasonable levels of general health in both groups, it is possible that subtle differences in cognitive ability and general health may have had an effect on the results of this study. The patients were slightly older than the controls, but only by a few years on average. Despite this, no association was found between age and average search time among either patients or controls. Likewise, despite the AMD group comprising more females than males, search durations and eye movement parameters did not differ between males and females. Another limitation of this study and a consideration for future work is the mapping of retinal sensitivity in these patients, perhaps with microperimetry. Finally, due to poor fixation, eye-tracking

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accuracy was worse for people with AMD than for controls. However, when the eye movement analysis was repeated, including only those who performed well during the calibration phase of the test, our results remained significant.

To conclude, some people with dry AMD, particularly those with geographic atrophy, have measurable difficulties on a computer-based "real-world" search task beyond those observed in visually healthy peers. This is likely translatable to difficulties that these patients may experience in their day-to-day lives; future work should investigate this further. The results of this work have important implications for the management of patients with dry AMD, particularly those who previously may have been assumed not to require the support of vision rehabilitation services. Visual search performance also may have potential to be used as a meaningful outcome measure for clinical trials for future potential treatments for dry AMD. A practically applicable version of the task we have illustrated in this study is the subject of future work.

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