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## ORIGINAL ARTICLE

# Tablet-based tests of everyday visual function in a diabetic macular oedema (DME) clinic waiting area: A feasibility study

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## Abstract

**Purpose:** (1) To assess the feasibility of conducting tablet-based vision tests in hospital clinic waiting areas; (2) To test the hypothesis that increasing severity of diabetic macular oedema (DME) is associated with the performance of tablet-based surrogates of everyday tasks and self-reported visual function.

**Methods:** Sixty-one people with mild ( $n=28$ ), moderate ( $n=24$ ) or severe ( $n=9$ ) DME performed two tablet-based tests of 'real-world' visual function (*visual search* and *face recognition*) while waiting for appointments in a hospital outpatient clinic. Participants also completed a tablet-based version of a seven-item, visual-functioning (VF-7) patient-reported outcome measure. Test performance was compared to previously published 99% normative limits for normally sighted individuals.

**Results:** Thirty-four participants (56%; 95% confidence interval [CI] 43%–68%) exceeded normative limits for visual search, while eight (13%; 95% CI 65%–24%) exceeded normative limits for face discrimination. Search duration was significantly longer for people with severe DME than those with mild and moderate DME ( $p=0.01$ ). Face discrimination performance was not significantly associated with DME severity. VF-7 scores were statistically similar across DME severity groups. Median time to complete all elements (eligibility screening, both tablet-based tasks and the VF-7) was 22 (quartiles 19, 25) min. Further, 98% and 87% of participants, respectively, reported the search task and face discrimination task to be enjoyable, while 25% and 97%, respectively, reported finding the two tasks to be difficult.

**Conclusions:** Portable tablet-based tests are quick, acceptable to patients and feasible to be performed in a clinic waiting area with minimal supervision. They have the potential to be piloted in patients' homes for self-monitoring.

## KEYWORDS

diabetes, diabetic eye disease, patient-reported outcome measures, quality of life, visual function

## INTRODUCTION

Diabetic eye disease is a leading cause of preventable vision loss in working age people,<sup>1</sup> affecting about one third of individuals with diabetes worldwide.<sup>2</sup> It is responsible for 6.4% of sight impairment and 5.3% of severe sight impairment

registrations in England and Wales.<sup>3</sup> Diabetic eye disease may be broadly classified into proliferative diabetic retinopathy (PDR) and non-PDR (NPDR), characterised by retinal neovascularisation. Diabetic maculopathy occurs when the macula is affected; this most commonly manifests as diabetic macular oedema (DME), where central vision loss results from

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thickening of the macula.<sup>4</sup> Both DME and PDR are considered sight-threatening forms of diabetic retinopathy.

The effect of diabetic eye disease on clinical and psychophysical measures of visual function has been previously documented (see Jackson and Barber,<sup>5</sup> for review). For example, Jackson et al.<sup>6</sup> reported impaired visual acuity (VA), contrast sensitivity, frequency doubling technology sensitivity and photopic and scotopic visual fields in patients with NPDR. In DME, VA is not always affected, depending on the distance of oedema from the macula.<sup>7,8</sup> However, the effect of these clinically detectable deficits on the ability to perform everyday tasks such as recognising faces or searching for objects, in DME, had not been explored. Reviews of the literature suggest that patients with diabetic retinopathy (DR) generally experience reduced health-related quality of life,<sup>9</sup> particularly in the vision-threatening stage of the condition.<sup>10</sup> Reviews specific to DME are not only limited, but also suggest reduced vision- and health-related quality of life.<sup>11</sup> Previous reviews have, however, focussed only on health- or vision-related quality of life rather than explore the full spectrum of possible impact, lacked rigorous systematic review methodology and been limited by the lack of empirical evidence at the time of their publication. Our recent systematic review<sup>12</sup> identified reading print, mobility, work, medication adherence, face recognition and watching television as tasks that people with DR have particular difficulties with. Yet, despite the differences in clinical presentation between DME and NPDR/PDR not involving the macula, research on the impact of DME specifically on everyday visual function is scarce. Moreover, there are several limitations to the use of patient-reported outcome measures (PROMs) alone to assess the impact of a condition of an individual's day-to-day life. First, questionnaire results may be affected by a range of psychological factors, such as personality and past experience, and are unlikely to reflect true functional ability. Second, they can be burdensome for the patient<sup>13</sup>; readability in particular can be an issue<sup>14</sup> and may exclude certain patient groups, leading to their underrepresentation in the literature.<sup>15</sup>

As the prevalence of DR and DME increases and treatments evolve, understanding the impact that these conditions have on the individual patient becomes increasingly important. One method of assessing 'real-world' visual function is by using self-report questionnaires about difficulty with tasks due to impaired vision. Traditionally, PROM questionnaires would be completed using pen and paper, but advances in technology have meant that PROMs are often now administered via computer, tablet or smartphone.<sup>16,17</sup>

Another method of testing a person's ability to perform everyday tasks is to observe them doing the task (or a surrogate measure of that task) and assess their performance. These are the most direct measures of assessing function, and often the least used.<sup>18</sup> Again, advances in technology have meant that everyday scenarios can be simulated using computer (e.g., tablet or virtual reality<sup>19,20</sup>)-based surrogates of real-world tasks; this type of test permits

### Key points

- Participants with diabetic macular oedema completed two portable tablet-based tests of everyday visual function. Visual search performance was significantly associated with diabetic macular oedema severity, whereas face discrimination did not show such an association.
- Self-reported visual function measured using the seven-item, visual-functioning tool was weakly correlated with better and worse eye visual acuity, but had no association with the severity of diabetic macular oedema.
- Tests were conducted in busy clinic waiting areas. This was found to be feasible and enjoyable for patients. These tests also have the potential to be piloted in home-monitoring schemes.

the researcher to observe a person performing a task designed to be as similar as possible to the same task in the real world, while allowing for a controlled experimental environment. A clear advantage of these methods is their objectivity. However, it is currently much more time-consuming to observe the performance of several everyday tasks (or surrogates of such tasks) than to ask about them in a questionnaire. Moreover, selecting which tasks are the most important to assess in a time-restricted situation can be challenging.

The concept of using tablet-based activities to productively utilise time patients spend in waiting areas is a growing area in both vision and other healthcare disciplines, for collecting questionnaire/PROM data,<sup>21,22</sup> as an educational tool<sup>23–26</sup> or for functional testing.<sup>27</sup> In this study, we aimed to assess the feasibility of conducting tablet-based tests of everyday visual function in hospital clinic waiting areas. We tested the hypothesis that increasing severity of DME is associated with performance on tablet-based surrogates of two everyday tasks: face discrimination and visual search. These tasks were selected because our previous work has shown that these are important everyday tasks that may be impaired in macular disease.<sup>28–30</sup> A secondary aim was to use the tablet to collect data on self-reported visual function of people with DME, again collected while the patient waited in a typically (pre COVID-19) busy hospital eye clinic, using a validated PROM.

## METHODS

### Participants

Participants were recruited consecutively between August and November 2019 from injection clinics and virtual DME clinics<sup>31</sup> at Moorfields Eye Hospital National Health Service

(NHS) Foundation Trust, London. Assessments were performed on a tablet computer while patients waited for their scheduled appointment in the busy hospital outpatient clinic (Figure 1).

Participants were required to be  $\geq 18$  years of age, have a diagnosis of DME in one or both eyes and be able to understand the consent process and instructions for study tests. Participants were excluded if they had macular disease in either eye due to causes other than DME, or any other ocular or systemic comorbidities that could affect visual function. In addition, patients were required to pass an abridged version of the Mini Mental State Evaluation,<sup>32</sup> which has been used in previous vision science research.<sup>29,30,33–35</sup> DME severity was graded (by author PJA) as mild, moderate or severe according to the International Clinical Classification of Diabetic Retinopathy: Severity of Diabetic Macular Edema scale.<sup>36</sup>

The study was approved by a NHS Research Ethics Committee and was conducted according to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant prior to taking part. Following participation, participant data were automatically anonymized, encrypted and saved on the tablet.

## Study tests

All tests were conducted on a Surface Pro 4 tablet computer (Microsoft, [Microsoft.com](https://www.microsoft.com)) containing a touchscreen measuring  $26 \times 17.3$  cm. The viewing distance was set at 50 cm from the screen at the start of each test (determined using a tape measure), although this was not strictly enforced during the test (no chin rest was used and patients were free to act naturally). Participants were tested binocularly, wearing their habitual correction for the specific viewing distance if available.



**FIGURE 1** Tests were conducted on a tablet computer while patients waited for their scheduled appointment in the busy diabetic macular oedema injection clinic. Image used with consent from identifiable individual.

Both tasks were described in detail elsewhere.<sup>37</sup> In the *face discrimination* task, participants were instructed to ‘spot the odd one out’ from among four human faces (Figure 2a). Participants performed 20 trials in total, and depending on whether they answered correctly or incorrectly on the previous trial, the degree of similarity between the faces was varied, using the QUEST adaptive algorithm (a commonly used maximum likelihood procedure).<sup>38</sup> The primary outcome measure was *face threshold*, that is, the smallest difference in facial features that participants were able to detect reliably. Face threshold was measured in units of dissimilarity,  $d$ , which express the Euclidean distance between the Standard and the just-noticeably-different Target face. Typical values for  $d$  fall between 3 and 4, with higher numbers indicating poorer performance.

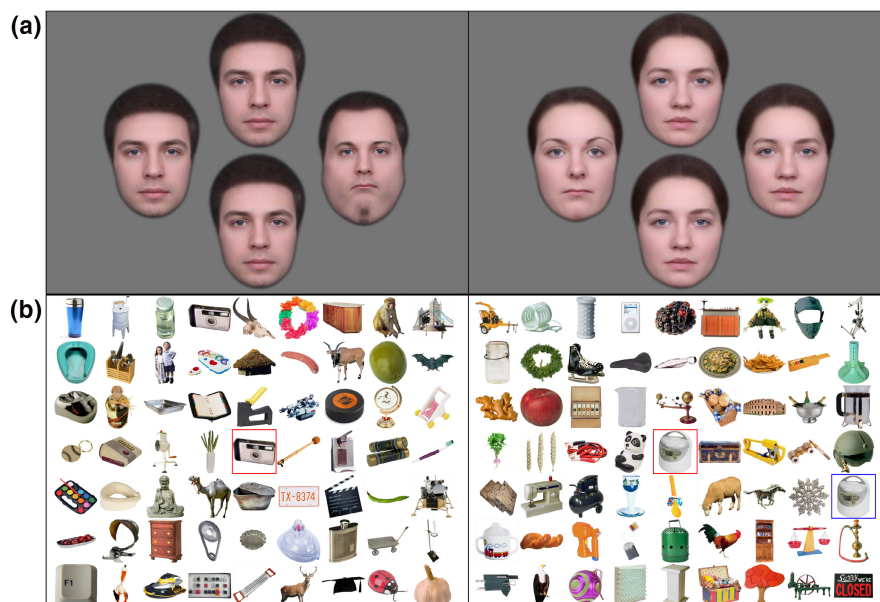
In the *visual search* task, participants were instructed to find a target item within a grid of photographs of everyday objects (Figure 2b). On each trial, a randomly selected reference image was presented in the centre of the screen inside a red square (Figure 2b). After 1 s, an additional 62 images were shown on the screen in a  $7 \times 9$  grid. One of these 62 images was the target image, identical to the reference image, and the participant was required to locate and touch the target image within the grid. During each trial, the reference image remained in the centre of the screen, so that participants were not required to memorise it, and could refer back it throughout the trial as required. This was repeated for 22 trials, with the target image shown at 22 set locations such that each of the locations within the array was tested once. The 22 target image locations were set following piloting and validation of the test as described in Jones et al.<sup>37</sup> Primary outcome measure for the search task was the median search time across the 22 trials. For further details regarding development and validation of the tablet tests, see Jones et al.<sup>37</sup>

In order to assess user acceptability of the tablet-based tasks, participants were asked to rate both how enjoyable and how difficult they found each of the tests using a five-point Likert scale. Participants were also asked to describe each test using three of their own words.

Participants also completed the seven-item, visual-functioning (VF-7) PROM.<sup>39</sup> This instrument asks participants to rate their difficulty with various everyday visual tasks including reading signs, recognising friends, reading, cooking and watching television, and has previously been validated for use in DR.

## Data analysis

Tablet-based test performance among groups of people with differing DME severity was compared to 99% normative limits, established previously in a population of young adults with healthy vision.<sup>37</sup> Median search time and face detection thresholds for participants in the mild, moderate



**FIGURE 2** Screenshots showing two trials from the tablet-based tests. In the face discrimination task (a) participants were required to identify the 'odd face out' from groupings of increasing similarity in order to establish a face threshold. In the visual search task; (b) participants found the target item (highlighted by a box in the centre of the screen) from an array of photographs of everyday objects.

**TABLE 1** logMAR visual acuity across diabetic macular oedema (DME) severity groups.

	Better eye VA	Worse eye VA
DME severity		
Mild DME	0.00 (−0.10, 0.00)	0.00 (0.00, 0.10)
Moderate DME	0.00 (0.00, 0.13)	0.10 (0.00, 0.23)
Severe DME	0.20 (0.10, 0.20)	0.30 (0.30, 0.40)
All	0.00 (−0.05, 0.10)	0.10 (0.00, 0.30)

Abbreviation: VA, visual acuity.

and severe DME groups were compared to this normative limit, and were also compared across groups using non-parametric tests. Median search duration at each of the 22 target locations was also examined, in order to investigate the relationship between target eccentricity and search duration.

Additionally, VF-7 scores were compared between DME severity groups. Associations were explored between main outcome measures (face discrimination; visual search performance and VF-7 score) and age, and better eye and worse eye logMAR VA.

## RESULTS

### Demographic and clinical data

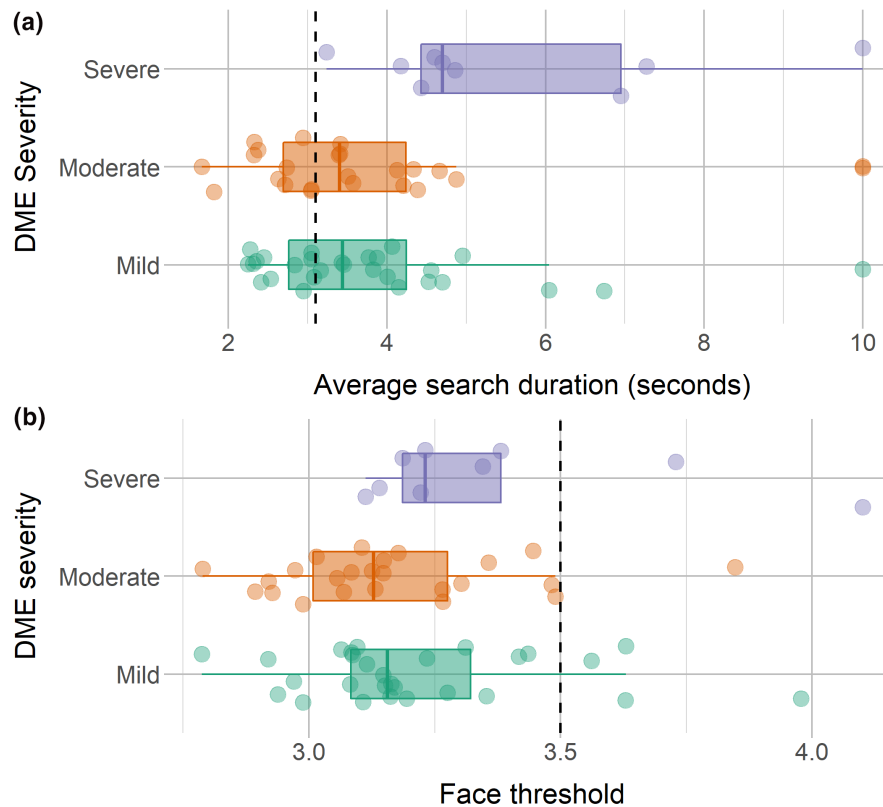
Sixty-one people (median [interquartile range; IQR] age 63 [56, 72] years; 41% female) classified as having mild ( $n=28$ ), moderate ( $n=24$ ) or severe ( $n=9$ ) DME completed both

tasks and the VF-7. Median (IQR) VA for each DME severity level and overall are shown in Table 1. When stratified by DME severity, people with severe DME had poorer VA (in both the better and worse eye) than those with moderate and mild DME; this was statistically significant (Kruskal–Wallis,  $p=0.001$  and  $p<0.001$  for better and worse eye VA, respectively). There was a relatively even split between those recruited from the virtual clinic ( $n=35$ , 57%) and from the injection clinic ( $n=26$ ; 43%). Most participants had active DME, with only six (10%) having inactive disease.

### Tablet-based test results

As shown in Figure 3, 34 participants (56%; 95% confidence interval [CI] 43%–68%) exceeded the normative limit for visual search, while eight (13%; 95% CI 65%–24%) exceeded the normative limit for face discrimination. Visual search duration was significantly longer for people with severe DME than for those with both mild and moderate DME (Kruskal–Wallis;  $p=0.01$ , Figure 3a). Face discrimination performance was not significantly associated with DME severity (Kruskal–Wallis;  $p=0.10$ , Figure 3b). Search duration (but not face discrimination) was significantly correlated with both the better eye VA (Spearman's  $r=0.39$ ,  $p<0.01$ ) and worse eye VA ( $r=0.50$ ,  $p<0.01$ ). None of the functional tests were significantly correlated with age (Spearman's  $r$ ;  $p>0.02$  for all).

Search duration was slower for more eccentric locations (see Figure 4). This association between search times and target eccentricity was significant for all groups (mild:  $r=0.15$ ,  $p<0.001$ ; moderate:  $r=0.16$ ,  $p<0.001$ ; severe:  $r=0.17$ ,  $p=0.01$ ).



**FIGURE 3** Box-and-whisker plots showing distribution of results for tablet-based functional tests (visual search in a, and face discrimination in b) stratified by diabetic macular oedema (DME) severity, with overlying data points showing results for each participant. The dashed line on each plot indicates the 99% normative limit for each test established by Jones et al.,<sup>37</sup> 3.10 s for visual search, and 3.50 d for face discrimination. d refers to units of dissimilarity, which express the Euclidean distance between the standard and the just-noticeably-different target face. Higher numbers indicating poorer performance.

## VF-7 results

Mean [SD] composite VF-7 scores (with higher scores indicating better self-reported visual function) did not differ significantly between patients graded as having mild (92.0 [14.4]), moderate (92.1 [10.1]) and severe (87.7 [8.8]) DME (all  $p > 0.05$ ). Better and worse eye logMAR VA were weakly correlated with the VF-7 composite score (Spearman's  $r = -0.36$ ,  $p < 0.01$  and  $r = -0.30$ ,  $p = 0.02$ , respectively). Better eye VA was also significantly correlated with individual items related to reading (newspaper size print [ $r = -0.30$ ,  $p = 0.02$ ]; small print in the telephone book [ $r = -0.43$ ,  $p < 0.01$ ]), while worse eye VA correlated with watching television ( $r = 0.32$ ,  $p = 0.01$ ) and reading newspaper print ( $r = -0.30$ ,  $p = 0.02$ ). The most frequently reported problem among all participants was difficulty reading small print in the telephone book (44% of all participants), while the least frequently reported problem was difficulty recognising friends (10% of all participants). Responses to VF-7 items stratified by DME severity are shown in Figure 5.

## Practicalities of tablet-based testing

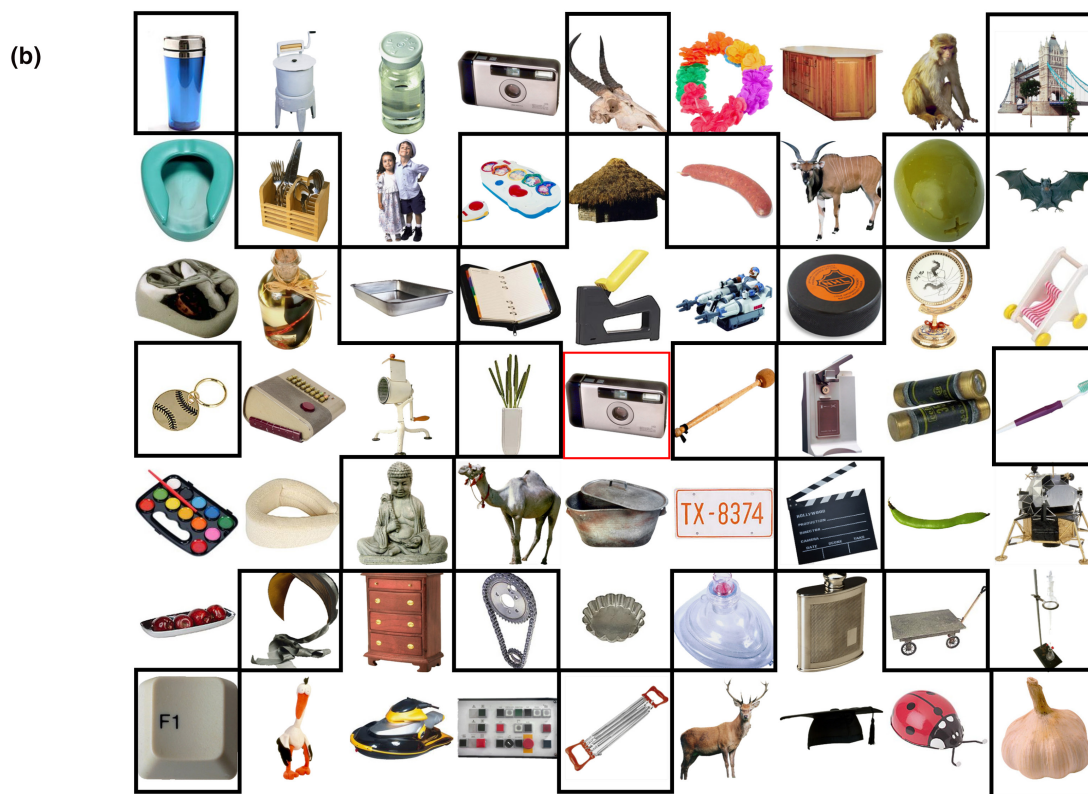
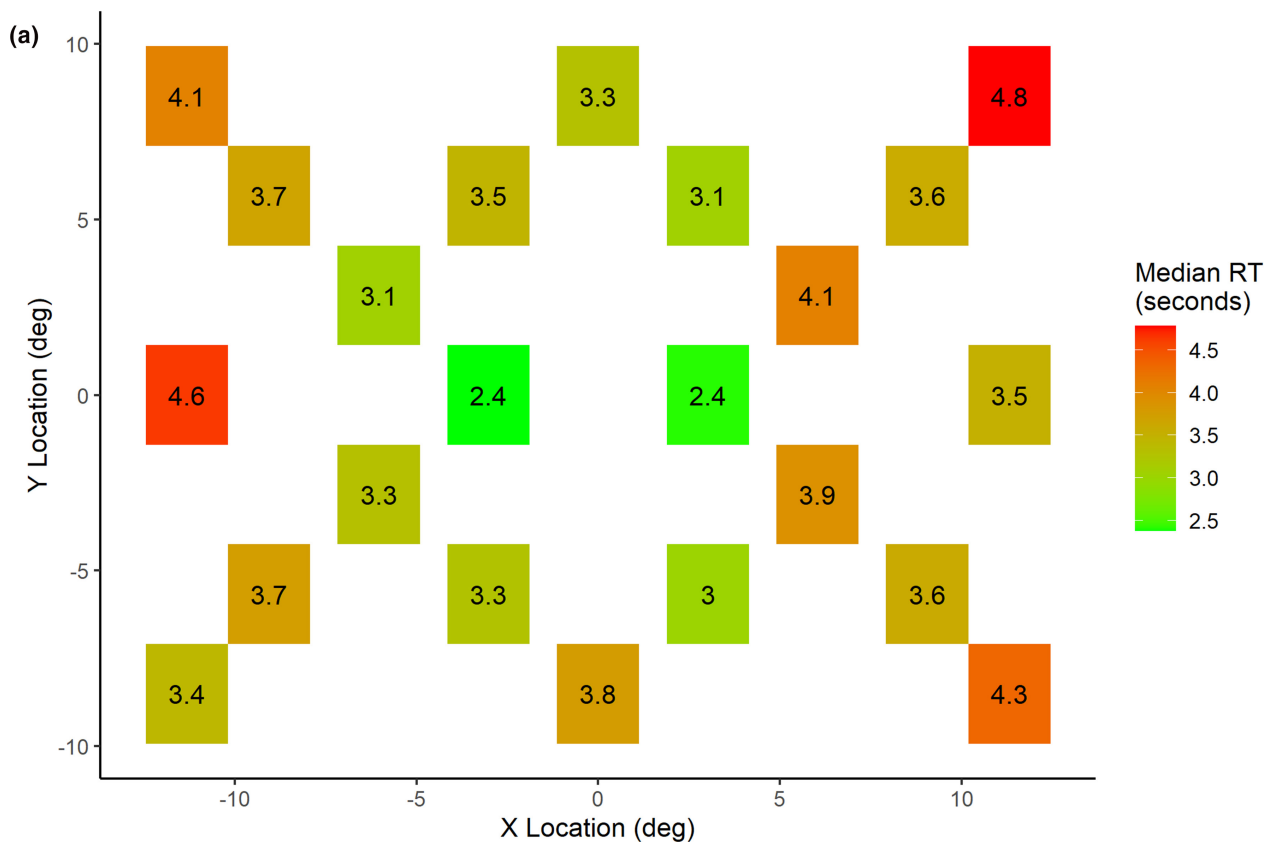
All 61 participants completed both tablet-based tasks and the VF-7. The median time taken to complete all of the

requirements, including study eligibility screening, both tablet-based tasks and the PROM, was 21.5 (IQR 19.1, 24.9) min. Further, 98% and 87% participants reported finding the search task and the face discrimination task to be *enjoyable*, respectively, while 25% and 97% reported finding the search task and face discrimination task *difficult*, respectively. The most frequently used words to describe the visual search task were 'easy', 'okay', 'good', 'fun' and 'enjoyable', while the most frequently used words to describe the face discrimination task were 'difficult', 'hard', 'challenging', 'good' and 'think'.

## DISCUSSION

### Summary of key findings

DME requires patients to attend regular lengthy hospital appointments, which often include considerable waiting time. We showed that this time can be used productively to measure patients' ability to perform everyday tasks of visual function, which could provide clinicians with information regarding how a patient's condition may impact their day-to-day activities. We demonstrated that these measurements could be made feasibly in clinic waiting rooms with minimal supervision. They also have the



**FIGURE 4** (a) Median response time (RT), in seconds, for the 22 target locations tested in the visual search task, averaged for all participants. Eccentricity in visual angle (degrees) was computed assuming a nominal viewing distance of 50 cm. The figure within each tile denotes the median search duration (in seconds) for that particular location across all participants. (b) The 22 test locations used for each trial, shown superimposed over an example trial for reference.

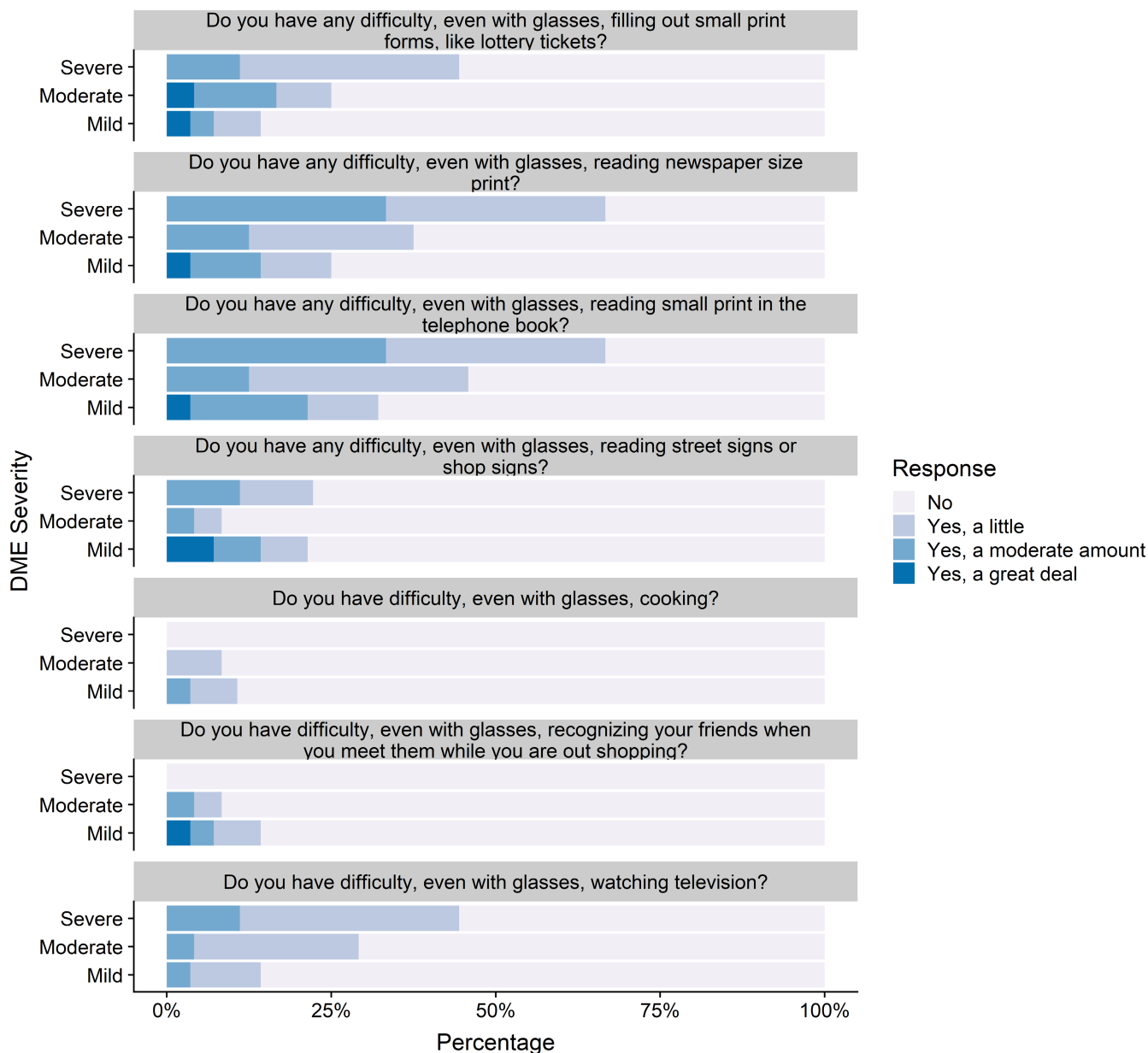


FIGURE 5 Responses to seven-item, visual-functioning questionnaire stratified by diabetic macular oedema (DME) severity.

potential to be used at home in between clinic appointments; a particularly useful application in the light of the rise in tele-ophthalmology use following the COVID-19 pandemic.<sup>40</sup> The tests are freely available online, are quick, provide useful data and were found to be acceptable to patients, with the majority 'enjoying' doing them. (The source code for the Faces test is freely available online for non-commercial use at: <https://www.bitbucket.org/iainwilson/facediscrimination>. The search test is freely available as an executable task for non-commercial use at: <https://github.com/CrabbLab/CrazySearch>). These measures are not intended to replace traditional clinical measures, such as VA. However, clinical measures alone are not sufficient to capture accurately how a disease impacts an individual's priorities, needs and day-to-day function.<sup>41</sup>

The results of this study showed that visual search duration increased with DME severity. This is noteworthy because previous research<sup>42</sup> has suggested visual search performance to be a useful indicator of mobility and ability to perform other everyday activities. No associations were found between DME severity and face discrimination performance. This was supported by responses to the VF-7 face recognition item within our cohort—this was the task that participants reported having the least difficulty with. Conversely, reading small print in the telephone book and newspapers was the most commonly reported difficulty. Interestingly, the face recognition and visual search performance results were in line with our previous findings for these measurements in age-related macular degeneration, despite the previous studies using different tests

and apparatus, and the age-related macular degeneration (AMD) cohort having a very different clinical and demographic profile.<sup>29,30</sup>

## Comparisons with previous literature

Evidence concerning the performance of everyday tasks with DME is scarce,<sup>12</sup> and what is known tends to come from self-report. For example, in a study of 546 treatment-naïve people with diabetic maculopathy,<sup>43</sup> just over one-third reported difficulties recognising faces. Results from qualitative studies also explored the difficulties that people with DME have with facial recognition,<sup>44,45</sup> and how this impacts their social interactions. Notably, difficulties typically occurred when viewing faces from a distance. Our tablet-based face recognition test did not elicit differences between DME severity groups, and perhaps a smaller viewing angle is required to reproduce these reported difficulties. However, our face recognition findings were supported by the self-report data; recognising friends was the least frequently reported problem recorded by the VF-7 among all of the DME participants. With regard to visual search, it has been shown in previous research that self-report of visual search in DME was comparable to visual search in AMD.<sup>46</sup> Therefore, while the present study is the first (to our knowledge) to measure visual search performance in DME, the findings are consistent with the wider literature.

Our tablet-based VF-7 PROM did not elicit any association between DME severity and self-reported visual functioning (based on either the composite or individual item scores). This contrasts with Gupta et al.,<sup>39</sup> who reported that VF-7 scores were associated with diabetic retinopathy, even after controlling for VA. This suggests that everyday visual function in diabetic retinopathy is not driven by VA alone. There are several possible explanations for these differences. First, the participants in Gupta et al.'s investigation had much poorer average VA than our participants (0.26 logMAR vs. 0.00 overall and 0.20 in the severe DME group in the present study). Second, while the focus of this study was on individuals with DME, Gupta et al. included participants with any form of DR, with no distinction between those with and without macular oedema. Moreover, both studies used different DME/DR classification systems. The results of the current study suggest that perhaps a PROM developed for use in DR as a whole may not be sensitive enough to detect subtle changes in visual functioning specific to DME. Alternatively, it is possible that VF-7 results in DME may be driven by visual function measurements not captured in this study, such as short wavelength perimetry or dark adaptometry.<sup>5</sup> Future studies should build on the work of Granström et al.<sup>44</sup> using qualitative research methodology to focus on discovering the symptoms and everyday experiences of individuals with DME. Computer adaptive testing may be

more appropriate than a PROM questionnaire, and work on developing and delivering such a tool in DR is already underway.<sup>47–49</sup> However, it is crucial that such work does not neglect the unique impact of DME.<sup>12</sup>

## Implications for research and clinical practice

The present study has shown that the use of tablet-based tests in eye care clinic waiting areas is acceptable, indeed enjoyable, to patients. Crucially, this could provide clinicians with important additional patient-relevant information prior to appointments, help with patient management and expectations and contribute to shared decision-making.<sup>50</sup> Crucially, this information could be used to highlight patients who may need additional support in terms of referral to low vision clinics, psychological services or Eye Clinic Liaison Officers. In the present study, patient perspectives of the tests were assessed using two simple questions. However, before such tests are introduced in clinic waiting rooms, it is crucial to conduct a full analysis of their acceptability to all users (including patients, clinicians and support staff), grounded in implementation theory, using a validated framework such as the Consolidated Framework for Implementation Research<sup>51</sup> or the Theoretical Framework of Acceptability.<sup>52</sup>

The tests also have the potential to be used as a tool for home monitoring; this should be the subject of future studies. While there is a relatively large and growing body of literature on the use of technology for home monitoring of ophthalmological conditions such as glaucoma<sup>53,54</sup> and AMD,<sup>55,56</sup> home monitoring in DR/DME has very little mention in the existing research literature. This seems strange given DR/DME patients are likely ideal candidates for a home-monitoring programme as many will already be accustomed to self-monitoring other aspects of their condition.<sup>40</sup> Moreover, the age demographic profile of DR/DME patients means that these individuals are likely to be more accepting of technology than those with age-related eye disease.<sup>57</sup> Indeed, studies on this topic are now beginning to emerge.<sup>58</sup>

When making decisions regarding future home monitoring of patients over time, a number of considerations need to be addressed. First, the frequency of administration—the literature on home monitoring of DME is in its infancy, but emergent studies of this condition<sup>58</sup> and other maculopathies<sup>59,60</sup> point towards a daily testing regimen being optimal. Qualitative research on other eye conditions suggests that patients may be highly motivated to undertake frequent home self-monitoring if it would mean any deterioration in vision could be detected and addressed sooner.<sup>61</sup> Conversely, others report finding more regular monitoring a challenge to keep up<sup>61</sup> and find it can contribute to greater awareness of their visual loss, leading to negative emotions.<sup>62</sup> Other considerations include availability of the devices to use at home. According to the recent review by Balaskas et al.,<sup>60</sup> administering

self-monitoring visual function tests via the patients' own smartphones or tablets has the potential to reach large numbers of individuals in a cost-effective manner. Yet challenges and questions remain to achieve and maintain optimal setup conditions, safe and effective data transfer and what would be considered a clinically meaningful change in test results.

These tests, which fall on the spectrum between very basic measures of visual function (e.g., VA, CS) and actual performance of everyday real-world tasks (e.g., recognising somebody in a shop or finding a particular product on a shelf), also have the potential to be used as secondary, patient-centred measurements in clinical trials. The latter could be important as trials are developed to provide evidence of new treatments improving or maintaining vision related quality of life.<sup>63</sup>

## Strengths and limitations

The mode of test delivery was a key strength of the present study; the tools underwent extensive testing and development in a laboratory-based setting<sup>37,64</sup> before successfully applying them in a real-world hospital. However, this was limited to centres within a single NHS hospital trust. Future work should focus on expanding delivery of tablet-based testing, with a particular focus, in the wake of the COVID-19 pandemic, on the self-administered use of tablet-based vision testing in patient's homes. Moreover, we did not collect additional clinical data (such as contrast sensitivity or colour vision), which might have been useful in these analyses. This should be the focus of future studies.

## CONCLUSIONS

Portable tablet-based tests are quick, acceptable to patients and can be feasibly performed in a busy clinic waiting area with minimal supervision. Composite scores from the VF-7 were not strongly associated with clinical measures of DME severity. Future work might involve in-depth interviews and focus groups to better understand the domains of visual function specifically affected by DME. With regard to performance-based tasks, the visual search task in particular has potential for providing clinicians with additional information about patient's functional deficits not indexed by conventional tests.

## AUTHOR CONTRIBUTIONS

**Deanna J. Taylor:** Formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); writing – original draft (equal). **Paolo J. Alquiza:** Investigation (equal); project administration (equal). **Pete R. Jones:** Formal analysis (equal); methodology (equal); software (equal); writing – review and editing (equal). **Iain Wilson:** Methodology (equal);

software (equal). **Wei Bi:** Software (equal). **Dawn A. Sim:** Conceptualization (equal); methodology (equal); supervision (equal); writing – review and editing (equal). **David P. Crabb:** Conceptualization (equal); methodology (equal); supervision (equal); writing – review and editing (equal).

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## CONFLICT OF INTEREST STATEMENT

DPC: consultant for Apellis; financial support from Allergan/Abbvie, Apellis, Santen; grant recipient from Allergan/Abbvie, Omikron, Janssen, Santen, Thea. All outside the submitted work.

## DATA AVAILABILITY STATEMENT

The datasets generated and analysed during the current study are available from the corresponding author on request.

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