Qualifying to Use a Home Monitoring Device for Detection of Neovascular Age-Related Macular Degeneration

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Importance Patients with intermediate age-related macular degeneration (AMD) using a home monitoring device have less loss of visual acuity, on average, at detection of choroidal neovascularization than do individuals using standard care monitoring techniques. Understanding the frequency with which patients are likely to initiate using a home monitoring device successfully is important in planning implementation of the device into practice.

Objectives To determine the frequency with which patients with intermediate AMD qualify to use a home monitoring device and to establish a reliable baseline reference value with the device to monitor their AMD for progression to choroidal neovascularization.

Design, Setting, and Participants Between October 8, 2010, and May 20, 2011, a total of 131 eligible participants within a university-based retina practice with intermediate AMD in the study eye and visual acuity of 20/63 or better completed an in-clinic qualification test for the home device. Intermediate AMD was defined as multiple intermediate-sized drusen or at least 1 large druse. If both eyes were eligible, the eye with better visual acuity was selected as the study eye. If both eyes had the same visual acuity, the patient used the eye with subjectively better vision. Analysis was performed between August 1, 2011, and January 11, 2014.

Main Outcomes and Measures The proportion of patients with reliable qualification test results and a test score predictive of successful home use of a monitoring device for detecting neovascular AMD, and the proportion who established a baseline reference value at home.

Results A total of 129 participants (98.5%; 95% CI, 96.4%-99.9%) had reliable qualification test results; 91 participants (69.5%; 95% CI, 61.6%-77.4%) who completed this test attained a score that suggested they would be able to successfully use the home device. Among the 91 participants who could initiate home testing, 83 did so, including 80 participants (87.9%; 95% CI, 81.2%-94.6%) who established a baseline value that could be used as a reference for future monitoring. Younger participants were more likely to qualify for home testing (mean [SD] age, 73.1 [8.4] vs 81.1 [7.1] years; P < .001). Visual acuity at study enrollment did not appear to be associated with successful qualification (mean visual acuity for those who did and did not qualify was 20/28 and 20/31, respectively; P = .10).

Conclusions and Relevance These data suggest that the in-office qualification test is a useful screening tool to identify patients who may benefit from the home device. In any given retina practice, our data suggest an estimated 61.6% to 77.4% of patients with intermediate AMD should be able to produce reliable initial test results in the office test using the home monitoring device and pass a qualification test to initiate home monitoring. Subsequently, 81.2% to 94.6% of patients should be able to establish a home baseline reference value for future monitoring.
choroidal neovascularization (CNV) from age-related macular degeneration (AMD) left untreated or unmanaged after substantial vision loss has occurred remains a leading cause of irreversible blindness in people aged 50 years or older throughout much of the world. In the United States, approximately 8 million people have intermediate AMD or monocular advanced AMD of whom 1.3 million people will develop advanced AMD during the ensuing 5 years. The prevalence of this at-risk population is expected to increase by more than 50% between 2004 and 2020.

The clinical features of AMD that can lead to vision loss can be divided into an intermediate stage and a late stage. Intermediate AMD is characterized by the presence of extensive medium-sized drusen or at least 1 large druse, while late AMD is characterized as geographic atrophy of the retinal pigment epithelium (RPE) and/or CNV typically involving the center of the macula.

Patients with intermediate AMD often have few or no symptoms. Patients who progress to late AMD may experience severe vision loss from sub-RPE, subretinal, or intraretinal fluid or hemorrhage; detachment of the RPE from the Bruch membrane; ingrowth of CNV from the choriocapillaris to the sub-RPE and subretinal space; subretinal fibrosis; and atrophy of the photoreceptors, RPE, and choriocapillaris. Detachment of the RPE from the Bruch membrane or detachment of the photoreceptors from the RPE may alter the normal vertical alignment of photoreceptors, causing metamorphopsia, a common symptom experienced by patients with CNV. Within days to months of the recognition of symptoms of CNV, patients may develop profound and irreversible vision loss. The incidence of CNV in an eye with intermediate AMD may range from 2% to 10% per year, depending on the extent of large drusen, the presence of pigmentary abnormalities, and the features of intermediate or advanced AMD in the other eye.

The standard care for management of CNV from AMD is repeated intravitreous antivascular endothelial growth factor therapy with aflibercept, bevacizumab, or ranibizumab. As treatment is likely to avoid moderate or severe vision loss, defined as at least a 3-line loss of visual acuity on a standard eye chart, in the majority of affected patients but results in at least a moderate vision gain in a minority of patients, initiation of antivascular endothelial growth factor therapy before substantial vision loss has occurred is important.

Eye care professionals often have relied on home Amsler grid testing to assist their patients in recognizing new symptoms that may indicate the onset of CNV. However, several studies have shown that the results of Amsler grid testing to detect CNV in patients with AMD have poor validity. The Preferential Hyperacuity Perimeter (PHP) test was designed to address some of the shortcomings inherent in using an Amsler grid to monitor for AMD progression and to try to detect CNV before moderate vision loss has occurred. A home monitoring device (ForeseeHome, Notal Vision Ltd) based on the PHP test was approved by the US Food and Drug Administration in 2009 as an aid for in-home monitoring of the progression of retinal abnormalities causing metamorphopsia, including, but not limited to, neovascular AMD (Figure 1).

The AREDS2-HOME (Age-Related Eye Disease Study 2-Home Monitoring of the Eye) study was a randomized clinical trial to determine whether home monitoring resulted in better visual acuity at the time of CNV lesion detection. Participants assigned to the home device demonstrated a smaller decline in visual acuity from baseline at the time of CNV detection compared with individuals assigned to standard care monitoring techniques.

To monitor AMD progression in the home setting using this device, patients must establish a baseline set of responses during a limited series of initial home testing. Outside the context of the AREDS2-HOME study, there is little known, to our knowledge, about the proportion of patients with high-risk nonneovascular AMD who may be able to incorporate the device successfully into their home monitoring regimen. The developers of the home device designed an in-office qualification test to identify individuals most likely to be able to use the device successfully at home. This report evaluates the utility of the qualification test to predict whether patients with high-risk AMD will be able to use the home device to establish reference values reliably so they may begin home monitoring for progression of AMD.

### Methods

#### Study Participants

Following approval by the Johns Hopkins University School of Medicine’s Institutional Review Board, eligible participants were identified by review of patient schedules and corresponding ophthalmic records from 2 retina specialists (S.B.B. and N.M.B.) within a university-based practice with the following criteria: age 55 years or older; only 1 study eye per participant was required to have intermediate AMD, as determined by the enrolling ophthalmologist; and visual acuity of 20/63 or better using an Early Treatment Diabetic Retinopathy Study chart. Intermediate AMD was defined as multiple intermediate-sized drusen or at least 1 large druse. If both eyes were eligible, the eye with better visual acuity was selected as the study eye. If both eyes had the same visual acuity, the patient used the eye with subjectively better vision.

Major exclusion criteria included macular pathologic conditions other than intermediate AMD. One hundred thirty-one participants with intermediate AMD in at least 1 eye were enrolled between October
In 2010 and May 2011. Potentially eligible study participants completed the written informed consent process and remained eligible if they were fluent in written and spoken English and they reported the ability to correctly use a standard computer mouse without assistance. Analysis was performed between August 1, 2011, and January 11, 2014.

In-Clinic Qualification Test: Reliability Parameters and Test Score
Study participants completed an in-office qualification test using their study eye and the home device. A standardized protocol was followed to perform the qualification test (see Appendix in the Supplement). The protocol included a short explanation by the study coordinator, an explanatory tutorial administered through the device, a trial or practice test administered through the device (an opportunity to mark areas of artificial distortion), a period for the participant to ask the coordinator questions, and the actual qualification test. This process, including the tutorial, took about 20 minutes per study eye; all participants were tested by a single coordinator (M.T.). Medical records were reviewed for all patients who completed an in-office qualification test to record baseline characteristics, such as participant age and sex, as well as visual acuity in the study eye.

Review of Patients Unable to Initiate Home Monitoring
Six months following completion of study enrollment, a retrospective review of the ophthalmic medical records, including imaging data when available, was performed for all patients who were unable to initiate home monitoring with the device (had unreliable test results, failed the qualification test, or did not establish a baseline) to determine how many eyes developed CNV.

Statistical Analysis
Data were analyzed with Excel 2007 (Microsoft Corporation) and Prism, version 5 (GraphPad Software, Inc). Descriptive analyses included the generation of means and standard deviations for variables of interest. Paired $t$ tests were applied to examine changes in the variables.

All $P$ values presented are based on 1-sided tests. All analyses were conducted using Excel 2007 (Microsoft Corporation).

Results
All 131 patients completed the in-office qualification test, of which 129 (98.5%; 95% CI, 96.4%-99.9%) had a reliable test score. Ninety-one (69.5%; 95% CI, 61.6%-77.4%) had a reliable test score and achieved a score at or below the threshold to qualify to initiate monitoring via the home device (Figure 2).

Baseline characteristics of the 91 individuals who qualified to initiate home testing are compared with the 40 participants who did not qualify (Table). Younger participants were more likely to qualify for home testing (mean [SD] age, 73.1 [8.4] vs 81.1 [7.1] years; $P < .001$). Visual acuity at study enrollment did not appear to be associated with successful qualification (mean visual acuity for those who did and did not qualify was 20/28 and 20/31, respectively; $P = .10$).

Establishing a Baseline
The 91 study participants who qualified to initiate home testing received the device at their home; 89 participants completed the setup of the device, while 2 elected not to participate. Five participants withdrew from the study after setting up the device but prior to performing their first home test session. One participant withdrew from the study after setting up the device and performing 2 home test sessions.

The remaining 83 participants (93.3%; 95% CI, 88.0%-98.5%) started the series of test sessions needed to attempt to establish a baseline value. In 74 of these participants (89.2%; 95% CI, 82.5%-95.8%), the average of their first 5 test scores was below the threshold score and they were judged able to establish a baseline. Eight participants had an average test score that met the criteria to extend the baseline test session number to 11 tests; 6 of these 8 participants were able to establish a baseline and continued home device monitoring.

Eighty of the 91 individuals who qualified (87.9%; 95% CI, 81.2%-94.6%) to initiate home test sessions did establish a baseline value, which would permit further monitoring for the development of neovascular AMD (Figure 2). Characteristics of the 3 individuals who did not establish a baseline value (after
Review of Patients Unable to Initiate Home Monitoring
Forty-three participants had unreliable test results, did not qualify for home monitoring, or failed to establish a baseline value. The minimum follow-up time was 1 month and the maximum follow-up time was 24 months. Of the 40 participants who had unreliable test results or did not qualify to initiate home monitoring, 2 subsequently developed neovascular AMD. The time from study enrollment to development of neovascular AMD was 10 and 12 months for the respective patients.

Of the 3 participants who qualified in the office to receive the device but failed to establish a baseline value during the initial test sessions at home, 2 developed neovascular AMD. The time from study enrollment to development of neovascular AMD was 4 months and 12 months.

Discussion
In this study performed within a university-based tertiary care retina practice, most patients with intermediate AMD and visual acuity with habitual correction of 20/63 or better were able to complete a qualification test with a reliable score when presented with a home device to monitor for the development of CNV. Of the patients who completed the in-office qualification test, 22.6% to 38.4% did not achieve a reliable score or a test score that suggested they would be able to use the home device to differentiate changes that might indicate incident CNV. These individuals were on average older than those who were successful at attaining a qualifying score, raising the possibility that these individuals may have had less familiarity or dexterity with rapid use of a computer mouse or other cognitive issues that may have affected their ability to take the test.

We were not able to identify an association with the level of visual acuity and individuals who did or did not qualify. As the individuals who did not qualify were not provided a device for home use, the extent to which the qualification test score truly predicted an inability for these individuals to use the home device and establish a baseline value successfully at home remains unanswered. If a study participant had 2 eligible eyes, a single eye was selected as the study eye; specifically, the eye with better visual acuity or with better subjective function was chosen when visual acuity did not differentiate between the 2 eyes. The rationale for this approach was the belief that if a patient could not pass the qualification test with the better-functioning eye, the patient most likely would not pass the test with the contralateral eye either. This failure to test each potentially eligible eye of an individual may have limited our estimates of the maximum proportion of patients who may have passed the qualification test.

Among the participants with eyes at high risk for developing CNV who achieved a qualification test score that suggested the device could be used to monitor their AMD for progression, our data suggest that 81.2% to 94.6% are able to establish a baseline from a series of 5 to 11 at-home tests. These findings are consistent with a relatively high predictive value of the qualification test itself to indicate candidates who likely will be successful in establishing home device monitoring.

While the enrollment criteria of the AREDS2-HOME study were similar to those of this study, seeking individuals with in-
termediate AMD in at least 1 eye and visual acuity of 20/63 or better, a large portion of the participants in the AREDS2-HOME study were also AREDS2 study participants. Among the 1,970 individuals screened to participate in the AREDS2-HOME trial, 450 (22.8%) were not eligible to enroll, owing largely to the reliability of the test score obtained at the in-office qualification test performed on the home device. The mean (SD) age of participants enrolled in the AREDS2-HOME trial was 72.5 (7.7) years. Among the patients in the AREDS2-HOME trial assigned to the home device, 105 eyes (8.0%) were unable to establish a baseline value with the device in the home setting. The AREDS2-HOME study design required participants to pass the qualification test in 1 eye, permitting individuals with 2 study eyes access to the device even though only 1 of their eyes may have been evaluated with the qualification test.16

Overall, the experience within our single-center cohort of consecutive patients who met the eligibility criteria and agreed to enroll within a university-based clinic provided confirmation that the results are similar to those obtained by the AREDS2-HOME study. The proportion of screened individuals who were eligible to initiate home device testing and the proportion who were successful in establishing a baseline value were similar between our study and that of the AREDS2-HOME study.

While older age is associated with a greater likelihood to fail the qualification test, we cannot determine at this time what other factors may influence the likelihood of qualifying to use the device or establishing a baseline value with the home device. Previous studies have shown that the phenomenon of preferential hyperacuity is resistant to variations in age.17 Thus, the methods of the PHP test most likely do not contribute to the reason why age affects the rate of qualification. The method of test administration, however, involves placing one’s head on the device hood to look onto the screen and use a standard computer mouse. These tasks require skills of advanced hand-eye coordination and balance that often deteriorate with age. Warabi et al18 described saccadic slowing and increase of total hand movement with aging that may explain the difficulty older patients had with passing the PHP qualification test. In addition, a patient may report that he or she can use a computer mouse without assistance, but the patient may not frequently use a mouse and may not possess the necessary dexterity to do so.

We explored the hypothesis that some of this study’s participants did not pass the qualification test because they already had CNV that was not detected clinically at the time of enrollment. A retrospective review of additional follow-up among participants who had unreliable test results, did not qualify, or failed to establish a baseline value identified only 4 of 43 individuals who subsequently were diagnosed with CNV lesions. In 3 of these individuals, the diagnosis was made nearly 1 year after they performed poorly on the qualification test, making it unlikely that CNV was present at the time of the test and accounted for the unreliable results. However, the duration of follow-up in these 43 individuals was limited (range, 1-24 months) and retinal imaging was not performed in any systematic fashion on these individuals, limiting our ability to explore this hypothesis more fully.

The strengths of this study include the prospective enrollment of consecutive patients who met the eligibility criteria and agreed to enroll within a university-based practice, with a standardized performance of the qualification test procedures, and complete follow-up of all participants who were provided with a device. The limitations include recognizing that all participants were from a tertiary retina referral practice at a university-based clinic, which may have had patients with a greater drive to pursue preventive monitoring strategies. Furthermore, we did not categorize the intermediate stage of AMD into more detail with respect to area of drusen or noncentral areas of geographic atrophy, which might have provided additional insight into failures to qualify. We did not have a sufficient number of cases that would provide a range of different amounts of drusen area or RPE abnormalities to determine confidently whether these findings were predictive of success with qualification.

Conclusions

Our findings, which are consistent with those of the AREDS2-HOME study, suggest that the qualification test within the office appears to be a good way of predicting which patients are likely to be successful at establishing a baseline value at home to initiate home monitoring. These data support the likelihood that a larger percentage of individuals at high risk of progressing to CNV from AMD who successfully complete a qualification test to use this home monitoring device will be able to establish a baseline value for subsequent monitoring at home. These individuals can continue to increase their chance of detecting neovascular AMD between scheduled office visits while the lesion is relatively small and associated with visual acuity that is relatively good.

Table. Baseline Characteristics of Study Participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Valuea</th>
<th>Did Not Qualify for Home Monitoring (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>73.1 (8.4)</td>
<td>81.1 (7.1)</td>
</tr>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤64</td>
<td>17 (18.7)</td>
<td>1 (2.5)</td>
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<tr>
<td>65-74</td>
<td>28 (30.8)</td>
<td>6 (15.0)</td>
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<tr>
<td>75-84</td>
<td>40 (44.0)</td>
<td>22 (55.0)</td>
</tr>
<tr>
<td>85-94</td>
<td>6 (6.6)</td>
<td>9 (22.5)</td>
</tr>
<tr>
<td>≥95</td>
<td>0</td>
<td>2 (5.0)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>41 (45.1)</td>
<td>19 (47.5)</td>
</tr>
<tr>
<td>Female</td>
<td>50 (54.9)</td>
<td>21 (52.5)</td>
</tr>
<tr>
<td>Visual acuity of qualification eyeb</td>
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<td></td>
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<tr>
<td>Snellen equivalent, mean</td>
<td>20/28</td>
<td>20/31</td>
</tr>
<tr>
<td>≥20/20</td>
<td>22 (24.2)</td>
<td>4 (10.0)</td>
</tr>
<tr>
<td>20/20 to 20/40</td>
<td>52 (57.1)</td>
<td>25 (62.5)</td>
</tr>
<tr>
<td>≤20/40 to 20/63</td>
<td>17 (18.7)</td>
<td>11 (27.5)</td>
</tr>
</tbody>
</table>

a Data are presented as number (percentage) of patients unless otherwise indicated.

b Visual acuity was measured with habitual correction and Early Treatment Diabetic Retinopathy Study charts. Snellen equivalents were recorded.

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REFERENCES

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