Visual acuity loss in patients with age-related macular degeneration measured using a novel high-pass letter chart

Nilpa Shah,1 Steven C Dakin,1,2 Sarah Dobinson,1 Adnan Tufail,1 Catherine A Egan,1 Roger S Anderson1,3

ABSTRACT

Background/aims Conventional Logarithm of the Minimum Angle of Resolution (logMAR) acuity is the current gold standard for assessing visual function in age-related macular degeneration (AMD). However, visual acuity (VA) often remains ‘normal’ when measured with these charts, even with advanced retinal changes. We wished to investigate how VA measurements with the Moorfields Acuity Chart (MAC), which employs high-pass filtered letters, compares to conventional letter charts in subjects with AMD.

Methods Monocular best-corrected VA measurements and test–retest variability (TRV) were compared for conventional and MAC charts in 38 normal observers (mean age 52.1 years) and 80 patients (mean age 80.6 years) with varying degrees of acuity loss owing to AMD. Methods of Bland–Altman and ordinary least-squares regression were employed for data analysis.

Results A proportional bias was confirmed between conventional and MAC measurements (r²=0.133, p=0.001) such that MAC acuity was −0.45 logMAR ‘worse’ at the 0.00 logMAR acuity level, but only −0.26 logMAR ‘worse’ at the 1.00 logMAR level. The mean bias was much smaller in the normal subject group (−0.16 logMAR). Similar TRV (ranging from ±0.09 to ±0.12 logMAR) was found for both charts in both subject groups.

Conclusions VA measurements with the MAC chart appear to be more sensitive to functional loss in AMD compared with conventional letter charts, with similar TRV. Simulations indicate this may be because the high-pass filtered letters are more vulnerable to undersampling as a result of retinal cell loss in the disease process.

INTRODUCTION

Age-related macular degeneration (AMD), the leading cause of blindness in the developed world, affects around 8.7% of the worldwide population, and this is projected to increase to 288 million in 2040 owing to a predicted exponential increase in population ageing. Patients with early AMD, characterised by the development of small-sized and medium-sized drusen or retinal pigment epithelial abnormalities, and those with intermediate AMD, characterised by medium and large drusen and/or geographic atrophy not involving the centre of the fovea, are often asymptomatic. It is usually the two forms of late AMD—geographic atrophy involving the fovea and neovascular AMD—that are most strongly associated with central vision loss.4–7

Several tests of visual function have been suggested as being appropriate in detecting macular disease and for monitoring progression. Contrast sensitivity has been demonstrated to be reduced in patients with drusen and good visual acuity (VA), and in particular this loss was found to be greatest at the high spatial frequency end compared with normal subjects.5–6 However, contrast sensitivity loss is not disease-specific and can be similarly affected by both optical and neural problems.

Studies investigating colour vision deficiencies7,8 and foveal flicker sensitivity9,10 have found conflicting results. Other studies have examined functional tests such as reading speed,11 photostress recovery,12 and microperimetry.13 However, in order to initiate effective preventative and therapeutic measures, it is important to possess a functional test that is specifically sensitive to changes in AMD while displaying good repeatability and must be easily understood by patients and easily administered in routine clinical settings.

The primary test used routinely in a clinical setting for assessing visual function in AMD is VA, and high-contrast VA is currently the only globally accepted end point for clinical trials for AMD therapies. VA is typically measured using a chart employing Logarithm of the Minimum Angle of Resolution (logMAR) design, such as the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, which is considered to be the current gold standard acuity test for monitoring AMD. Traditional VA charts use black alphabetic letters on a white background and have the advantage of a low guess rate owing to the large number of alternatives from which the observer can choose. For the purposes of detecting refractive error, they have been shown to be sensitive to optical defocus as a result of spatial frequency phase reversals.14 However, these conventional letters appear to be relatively poor indicators of visual loss in early and intermediate age-related macular disease.4,15 Klein et al16 reported a decrease in VA of only two or fewer letters for patients displaying early age-related maculopathy lesions compared with eyes without such early lesions. Given that, even in the absence of any clinical change, test–retest variability (TRV) of between ±0.07 and ±0.19 logMAR lines has been observed,17–22 with higher variability in patients with AMD,23 this level of visual deficit cannot be reliably detected and is therefore not diagnostically meaningful. Even in advanced disease, VA can often remain normal until the fovea is observably affected. Most
choroidal neovascular membranes have been shown to originate eccentrically and therefore have little impact on VA initially. There appears to be a weak relationship between the severity of retinal changes and VA and this is influenced by the location of the lesion and the extent of the lesion in addition to the stage of the pathology.

Initial work by our group has demonstrated that acuity thresholds, measured using pseudo-high-pass filtered letters, yield improved test-retest repeatability over conventional black-on-white letters while displaying greater robustness to the effects of optical defocus in normal subjects. In these stimuli, initially described by Howland et al., the low spatial frequencies, where there are large inter-letter differences, are effectively removed. They appear as letters with a black ‘core’ and a white surround, the mean luminance of which is equal to the grey background on which they are presented. Detection and recognition thresholds for these letters are almost identical under foveal viewing conditions in normal subjects, meaning the letters disappear soon after the resolution limit is reached, hence the term ‘vanishing optotypes’. However, under extrafoveal viewing conditions, we have demonstrated that this is not the case and the two thresholds are significantly different, indicating that, while detection is limited by the filtering effects of the eye’s optics, recognition thresholds may be limited by the underlying neural sampling density. The Moorfields Acuity Chart (MAC) is a new chart employing these letters and we wished to investigate, for the first time, how VA using the MAC compares to that measured using conventional letter charts in both normal subjects and patients with AMD.

MATERIALS AND METHODS

Four different VA test charts were employed. These charts have been described in detail in a previous study, but in essence, two of them, here termed Conventional charts 1 and 2 (C1 and C2), followed the design of ETDRS charts 1 and 2 using the 10 Sloan letters in conventional black-on-white letter design. Figure 1A shows the appearance of C1. The other two charts, termed the Moorfields Acuity Charts 1 and 2 (MAC1 and MAC2), were of identical layout except that they employed a high-contrast, high-pass letter design with a grey background of the same mean luminance. Figure 1B shows the appearance of MAC1. The white components of each chart had a luminance of 114 cd/m² and the grey background of the high-pass charts was 50.5 cd/m². The VA range, based on the total angular width of one letter limb from a 4 m test distance, was 1.20 logMAR (3.8/60) to −0.20 logMAR (6/3.8) for all charts. Our previous studies have shown that, because of the removal of lower frequencies, acuity threshold measurements obtained using high-pass filtered letters are, on average, larger than those attained with conventional letters. With this in mind, and since the charts were designed for use in an AMD population, an additional two lines (1.1 and 1.2 logMAR) were included at the top, and one line (−0.3) omitted from the bottom of each chart.

Ninety normal subjects (35 males) of ages ranging from 20 to 84 years (mean 46.8 years) were recruited from a primary care optometric practice and from the staff at Moorfields Eye Hospital. In addition, 80 participants (36 males) with a range of visual acuities owing to macular degeneration diagnosed in an outpatient retinal therapy clinic at Moorfields Eye Hospital with ages ranging from 59 to 95 (mean 80.6 years) were recruited.

Each subject underwent preliminary screening tests, both to verify their eligibility to participate in the study and for phenotyping purposes. The inclusion criteria for this study for the normal subjects was best-corrected VA no worse than 0.20 logMAR and no significant ocular pathology and that for the AMD group was no significant ocular pathology other than AMD, classified using the Age-Related Eye Disease Study (AREDS) grading system. Both groups underwent baseline refraction at 4 m (retinoscopy and subjective) with mean spherical refractive error found to be −0.65 D (range −6.75 to +3.50) and +0.23D (range −2.25 to +4.25) for the normal and AMD observers, respectively, and ocular examination using binocular indirect ophthalmoscopy.

Following the preliminary screening tests, best-corrected monocular VA was measured using each of the four charts; C1, C2, MAC1 and MAC2, which were presented in a random order to reduce any effects of fatigue and learning. For the normal subjects, the test eye was randomised and, in the AMD group, the eye with the poorest VA was selected. The mean C1 VA for the normal subjects was −0.07 logMAR (range −0.20 to 0.26 logMAR) and that for the AMD subjects was 0.45 logMAR (range −0.02 to 1.20 logMAR). In the AMD group, eight subjects were classified as having early AMD (AREDS category 2) with C1 acuity ranging from −0.02 to 0.28 logMAR, eight with intermediate AMD (AREDS category 3) with C1 acuity from 0.12 to 0.52 logMAR and the rest with advanced AMD (AREDS category 4) with C1 acuity from 0.02 to 1.2 logMAR.

Each subject was asked to read each letter from the top of the chart in a forced choice procedure whereby they were required to guess the letter if they were unsure of the letter identity. Viewing time was not restricted and testing was terminated when four or more errors were recorded on a single line, with responses recorded on a proforma data sheet. VA scores were then calculated on a by-letter basis where each letter was assigned a value of 0.02 logMAR and the final score was calculated as 1.3−0.02*number of letters read correctly.

Statistical analysis

Frequency distribution graphs were used to confirm that the difference in the two acuity measurements with each chart type was mostly normally distributed. The methods of Bland–Altman were applied to analyse the mean bias with TRV expressed as the 95% limits of agreement for the two test chart types in each group of subjects. The methods of Bland–Altman do not quantify any potential proportional bias so where appropriate, ordinary least-squares regression analysis was used. The GraphPad Prism statistical analysis package (GraphPad Software, La Jolla, California, USA) was employed for this purpose.

RESULTS

Mean C1 acuity was found to be −0.07 logMAR (range −0.20 to 0.26 logMAR) for the 90 normal subjects and 0.45 logMAR (range −0.02 to 1.20 logMAR) for the 80 AMD subjects.

Linear regression analysis was first used to investigate the effect of age on the difference in acuities measurements using the MAC1 chart compared with the C1 chart in the 90 normal subjects plotted with open symbols (figure 2). A small but statistically significant proportional bias was found such that the difference between the two tests increases with age (r²=0.062, p=0.018, dashed line), but the 95% CIs for the slope only just miss zero (−0.0021 to 0.0002). In order to consider any potential ceiling effect of subjects not reaching the full termination criterion (four or more errors) in this group on the conventional letter charts, a separate analysis was conducted on 38 subjects, with ages ranging from 20 to 84 years (mean 52.1 years), who met the full termination criterion. Mean C1 acuity for this group was found to be 0.00 logMAR (range −0.12 to 0.26 logMAR). It can be seen that, although as in
previous studies the MAC charts display ‘poorer’ acuity, this systematic bias is similar for subjects who strictly met the termination criterion and those who did not. There is also no statistically significant proportional difference between the two measurements. \( r^2 = 0.026, p = 0.334, \) solid line.

Bland–Altman scatter plots were then constructed to graphically present the distribution of results for the C1/C2 and MAC1/MAC2 for both the 90 normal and 80 AMD subjects. Since no significant difference between the two tests was found with increasing age, all ages were included for the normal group. The differences were assumed to be normally distributed using the Shapiro–Wilk W test \( (p = 0.064 \text{ for C1 and C2 in the normal group; } p = 0.092 \text{ for C1 and C2 in the AMD group; } p = 0.070 \text{ for MAC1 and MAC2 in the AMD group}) \) except for the MAC1 and MAC2 in the normal group \( (p = 0.006) \). A frequency distribution plot (not shown) however, showed no gross deviation from normal, and therefore, on this basis, we felt justified in using Bland–Altman summary statistics of mean bias and TRV 95% limits of agreement.

For the normal subjects, when all 90 participants are considered, the mean bias was \(-0.01\) logMAR between C1 and C2 and \(0.00\) logMAR between MAC1 and MAC2. The TRV was found to be \(\pm 0.09\) logMAR for C1/C2 and \(\pm 0.11\) logMAR for MAC1/MAC2. The mean difference between C1 and MAC1 was found to be \(-0.14\) logMAR. However, once again to exclude any potential ceiling effect of the chart termination criterion, particularly for the conventional letter charts, only those 38 normal subjects who strictly displayed four or more errors were further analysed.

Figure 3 displays the Bland–Altman scatter plots to graphically present the distribution of results for the C1 and C2 charts (figure 3A) and MAC1 and MAC2 charts (figure 3B) for the 38 normal subjects who met the full termination criteria \( (\text{data set in green}) \) and 80 AMD subjects \( (\text{data set in orange}) \). These plots show the TRV for each measurement technique \( (\text{here, } 1.96 \times \text{SD of the difference}) \) alongside the mean differences, which are summarised in table 1. There was no evidence of any systematic association between the level of agreement and the underlying acuity. The variability of the conventional charts was found to be similar compared with the MACs in the normal subjects \( (\text{two-tailed } p = 0.10, F_{37,37} = 1.531) \) but was determined to be statistically different in the AMD group, the MAC displaying a lower TRV \( (\text{two-tailed } p = 0.10, F_{79,79} = 1.336) \).

Figure 3C displays the comparison results for the different charts for the AMD group, and from this a proportional as well as a systematic bias can be inferred in that a greater level of disagreement between the two chart types exists at the ‘better’ acuity end. To investigate this, we performed ordinary least-squares regression analysis on the data, confirming the presence of the bias \( (r^2 = 0.133, p = 0.001) \). The difference in VA between C1 and MAC1 was \(-0.45\) logMAR at the \(0.00\) logMAR level, indicating that conventional VA measurements were on average \(4.5\) logMAR lines ‘better’ than high-pass acuity measurements compared with a difference of only \(-0.26\) logMAR \( (\text{approximately two and a half lines}) \) at the \(1.00\) logMAR acuity level. When we look at the 38 normal subjects with good VA \( (\text{figure 3D}) \), we find the mean bias between the two test types is much smaller at \(-0.16\) logMAR \( (\text{approximately one and a half lines}) \).

**DISCUSSION**

The performance of any clinical test is determined by both the variability within the test—the test noise—and the strength of the disease ‘signal’ that it is measuring. Detectability can be
improved by redesigning the test to either decrease the TRV or boost the disease signal.

ETDRS VA measurements are considered to be the current gold standard for monitoring functional changes in acuity in patients with AMD. While these tests have demonstrated an improvement over previous commonly used VA tests such as the Snellen chart, resulting in a greater ability to monitor change and thus the ability to detect disease onset and progression, they are still poor at reflecting the true status of the visual system in AMD with good VA being reported in even advanced disease.

Figure 3C demonstrates a proportional bias, indicating that the difference between the two chart measurements was larger in the AMD subjects with better acuity. This difference was found to be approximately 4.5 lines at the better acuity end (around 0.0 logMAR) for patients with AMD compared with a difference of just over 1.5 logMAR lines in normal subjects with similar acuity levels. This suggests that the MAC chart is able to detect functional loss owing to AMD at acuity levels where ETDRS acuity remains relatively unaffected. Our previous study that measured acuity in normal subjects with uncorrected refractive error found a difference of approximately 2 logMAR lines at the good acuity end, similar to the difference found for the normal subjects in this study.

The difference at the poorer acuity end in the present study, as a result of neurological loss, was also found to be larger than

Table 1  Bland–Altman summary statistics of mean bias and TRV expressed as 95% limits of agreement

<table>
<thead>
<tr>
<th></th>
<th>Mean difference (SE)</th>
<th>95% CI mean difference</th>
<th>Range of observed difference</th>
<th>TRV 95% limits of agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal subjects (n=38)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C1–C2</td>
<td>−0.011 (0.008)</td>
<td>−0.027 to 0.005</td>
<td>−0.12, 0.12</td>
<td>±0.093</td>
</tr>
<tr>
<td>MAC1–MAC2</td>
<td>−0.009 (0.008)</td>
<td>−0.026 to 0.008</td>
<td>−0.12, 0.08</td>
<td>±0.103</td>
</tr>
<tr>
<td>AMD subjects (n=80)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C1–C2</td>
<td>−0.019 (0.007)</td>
<td>−0.033 to −0.005</td>
<td>−0.20, 0.12</td>
<td>±0.123</td>
</tr>
<tr>
<td>MAC1–MAC2</td>
<td>0.009 (0.005)</td>
<td>−0.001 to 0.019</td>
<td>−0.08, 0.14</td>
<td>±0.090</td>
</tr>
</tbody>
</table>

AMD, age-related macular degeneration; MAC, Moorfields Acuity Chart; TRV, test–retest variability.
the difference attributed to optical factors in our previous study\(^3\) (−0.26 logMAR vs −0.05 logMAR). This suggests that the MAC may be better able to differentiate between VA loss resulting from neural versus optical deficits and may display higher sensitivity in detecting functional changes as a result of neural loss in AMD.

However, while the MAC may result in a stronger ‘disease signal’, this is of little value if it is lost in the test variability. The TRV was found to be similar across both charts in both subject groups. In line with previous studies, we found that the conventional letter charts demonstrate statistically significantly poorer TRV in subjects with AMD compared with normal subjects (±0.12 vs ±0.09 logMAR); however, clinically this may not be significant. The TRV attained with the MAC seemed to be quite unaffected by the presence of disease (±0.10 vs ±0.09 logMAR). This is comparable to the value of ±0.10 logMAR found in a previous study\(^3\) by our group, in which TRV was measured in 50 normal subjects with uncorrected refractive error with these charts.

But why should the MAC display higher sensitivity to visual loss in AMD? It has long been known that, for foveal vision in the normal, healthy eye, visual resolution is limited by the low-pass filtering effects of the eye’s optics such that spatial frequencies higher than the resolution limit of the retinal mosaic (Nyquist limit) do not pass through.\(^3\) If we view the charts back figure 1 at a reasonable distance (around arm’s length), it can be observed that the smaller letters do indeed vanish on the MAC soon after the resolution limit is reached and the difference in resolution between the two charts is only around 1–2 lines. However, as the eye ages, AMD develops and photoreceptors begin to drop out, resulting in holes in the retinal sampling mosaic, it is reasonable to assume that the neural sampling density, rather than optics, will quickly become the ‘weak link’ in the chain of visual processing.

The upper panels of figure 4A,B simulate the two chart types after they have been sampled by a noisy, slightly reduced-density, ‘non-tiling’ sampling array, as might be expected in AMD. It can be observed that there is now a much greater difference in the resolution limit between the two charts, with the MAC suffering more at the hands of undersampling. In other words, for conventional letters, a larger proportion of photoreceptors in the fovea must become dysfunctional in AMD compared with vanishing optotypes before the loss becomes apparent. There is also a greater loss of apparent contrast in this ‘neural image’, further

**Figure 4** Image of (A) conventional and (B) Moorfields Acuity Chart (MAC) chart sampled by a reduced density sampling array to schematically represent what may be perceived in age-related macular degeneration (AMD). (C) and (D) show the conventional and MAC chart, respectively, sampled with a further reduced density array to represent what may be perceived when AMD affects the fovea.
degrading performance. Interestingly, there now are letters towards the bottom of the chart that remain readily detectable but not resolvable. This simulation would predict that the high-pass letters no longer behave as ‘vanishing optotypes’ in the fovea when neural sampling density reduces sufficiently, and the detection and resolution limits begin to separate. This has previously been observed in extrfoveal vision for high-pass letters.29 39 40

When sampling density reduces further as the fovea becomes more involved (figure 4C,D), the recognition of both charts starts to suffer in a more equal fashion, explaining why the difference in acuity loss between the charts becomes smaller. However, it is now very obvious that the high-pass letters remain detectable long after the resolution limit is reached and they no longer vanish.

To test this idea experimentally, we further employed a subset of subjects to separately measure detection and recognition performance for the high-pass letters. This subgroup had ETDRS acuity ranging from −0.14 to 0.64 logMAR and consisted of 9 normal participants (mean age 75.3, range 69–81 years) and 20 patients with AMD (mean age 79.3, range 70–90 years). Of these, 3 had early AMD (AREDS category 2) with VA ranging from −0.10 to 0.20 logMAR, 2 had intermediate AMD (AREDS category 3) with VA −0.04 and 0.12 logMAR and 15 had advanced AMD (AREDS category 4) with VA ranging from 0.10 to 0.64 logMAR. Stimuli, generated using MATLAB V7.6 (MathWorks, Cambridge, UK), were presented on a high-resolution (1280×1024 pixels) Dell Trinitron P992 CRT monitor (Dell Corp., Bracknell, Berkshire, UK) at 4 m with a background luminance of 53.6 cd/m². Detection acuity was measured using a temporal two alternative forced choice (2AFC) procedure where the subject had to indicate which interval contained the stimulus. For the recognition task, a spatial 10 AFC procedure was employed where the subject had to verbally indicate the identity of the letter. The algorithm employed a QUEST procedure where the size of any displayed letter is determined by knowledge of the previous responses, using the same 10 letters as the MAC chart, converging on a 75% correct end point. Results are plotted in figure 5. It can be seen that, at the good acuity end, there is little difference in detection and recognition thresholds, although there is some expected disparity in the two thresholds as a result of the difference in guess rate as a result of the difference in nAFC for the two tasks.

However, as acuity worsens as a result of AMD, it can be seen that the difference between the two thresholds increases such that the subject can detect contrast in the stimulus but is unable to veridically resolve the letter, that is, the letters no longer behave as ‘vanishing’ optotypes. This finding serves to support the notion that undersampling as a result of photoreceptor loss underlies the acuity loss in AMD and confirms the undersampling simulation’s prediction that detection and recognition thresholds will increasingly separate, with recognition declining faster, as vision worsens owing to AMD, meaning that foveal vision increasingly behaves in the same manner as parafoveal vision.

This increasing separation of detection and resolution with the MAC as AMD develops may, in itself, provide insight into the development of AMD, but will require further experimental investigation.

In conclusion, VA measurements taken with the MAC appear to be more sensitive in detecting functional loss in AMD compared with conventional letter design charts, with similar TRV. This earlier detection will be of increasing importance as more treatments for AMD become available. To our knowledge, this is the first high-pass filtered letter acuity chart following the logMAR ETDRS chart design and testing protocols, which has been validated in patients with AMD. We chose to employ letters that closely matched the design of Howland et al.31 32 Future research could perhaps examine performance with letters containing different frequency bands; indeed, the Cardiff Acuity Test cards are effectively high-pass filtered at a higher ‘cut-off’ relative to the target size. However, the problem with doing this on a logMAR-style chart is that the letters would need to be considerably larger to be resolved, leading to practical chart design problems and an even greater scaling difference in acuity relative to a conventional chart. It should be noted, however, that both the MAC and Cardiff Acuity Test targets are really only pseudo-high-pass filtered in order to maintain a square-wave appearance and high contrast in the luminance profile, and this further limits the range of possible high-pass filtering ‘cut-offs’.

**Contributors** Study concept and design: NS, SCD, RSA. Acquisition, analysis or interpretation of data, critical revision of the manuscript for important intellectual content, final approval of the version to be published, accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: all authors. Drafting of the manuscript: NS, RSA.

**Funding** This research was supported by a Fight for Sight studentship and by the Special Trustees of Moorfields Eye Hospital NHS Foundation Trust (grant number 1973).

**Competing interests** NS and RSA and SCD—co-inventor of Moorfields Acuity Chart.

**Ethics approval** West London Research Ethics and all procedures adhered to the tenets of the Declaration of Helsinki.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**REFERENCES**


---

**Figure 5** Plot of visual acuity against the difference between recognition and detection values for 9 normal (green circles) and 20 age-related macular degeneration (AMD) (orange diamonds) subjects. Linear regression analysis is plotted for the AMD group only (orange dotted line with $r^2=0.4523$) and for all subjects (black dotted line with $r^2=0.3986$). LogMAR, Logarithm of the Minimum Angle of Resolution.

Clinical science


18 Vanden Bosch ME, Wall M. Visual acuity scored by the letter-by-letter or probit methods has lower retest variability than the line assignment method. Eye (Lond) 1997;11(Pt 3):411–7.


Visual acuity loss in patients with age-related macular degeneration measured using a novel high-pass letter chart

Nilpa Shah, Steven C Dakin, Sarah Dobinson, Adnan Tufail, Catherine A Egan and Roger S Anderson

Br J Ophthalmol published online February 4, 2016

Updated information and services can be found at: http://bjo.bmj.com/content/early/2016/02/04/bjophthalmol-2015-307375

These include:

References

This article cites 40 articles, 14 of which you can access for free at: http://bjo.bmj.com/content/early/2016/02/04/bjophthalmol-2015-307375#BIBL

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections

Articles on similar topics can be found in the following collections

Retina (1569)

Notes

To request permissions go to: http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to: http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to: http://group.bmj.com/subscribe/