Frequency of visual field testing when monitoring patients newly diagnosed with glaucoma: mixed methods and modelling

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Scientific summary

Visual field testing for monitoring newly diagnosed glaucoma

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Background

People with glaucoma represent a major workload of UK NHS eye services. Comprehensive guidelines for the diagnosis and management of glaucoma were published by the National Institute for Health and Care Excellence (NICE) in 2009, revealing an absence of research evidence about how patients with the condition should be monitored over time. The NICE Guideline Development Group published a few important recommendations for essential future research and their very first question was:

> *. . . What is the clinical effectiveness and cost effectiveness of using different monitoring intervals to detect disease progression in people with glaucoma who are at risk of progression? . . .*
>
> *NICE.* Diagnosis and Management of Chronic Open Angle Glaucoma and Ocular Hypertension. NICE Clinical Guideline 85. *Manchester: NICE; 2009*

The importance of this question is emphasised further by the statement:

> *. . . The answer to this question is key to recommendations on chronic disease monitoring intervals . . .*
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> *NICE.* Diagnosis and Management of Chronic Open Angle Glaucoma and Ocular Hypertension. NICE Clinical Guideline 85. *Manchester: NICE; 2009*

A randomised comparative trial (RCT) of different monitoring intervals was suggested; this would be a major undertaking, but a RCT would probably provide better evidence on a range of issues related to NHS glaucoma management. The purpose of the current project was to explore NICE's question by using existing NHS data on current practice and to provide new research knowledge through modelling. The audit and modelling work described in this study is an important step towards planning a RCT and justifying the cost of such a study. This research is, therefore, concerned with identifying glaucomatous deterioration ('progression') in a manner that is worth the cost. This project focused on the mainstay measurement for glaucoma monitoring, visual fields (VFs).

Glaucoma management aims to preserve the patient's vision and vision-related quality of life. Tests of vision, such as the VF test, are, therefore, of considerable clinical importance, and continue to be the yardstick for detecting and monitoring glaucoma in clinical practice. VF testing (also known as perimetry) aims to locate damaged areas in a patient's field of vision using an automated machine that systematically measures the patient's ability to identify the presence of a small spot of light at different locations in their VF. Glaucoma patients must be monitored regularly for progression in their vision because perimetry measurements are very variable ('noisy'), which means that frequent monitoring, perhaps over a long period of time, is required to accurately detect true disease progression.

The number of VF tests required to detect disease progression is often overlooked. It is essential to detect rapid VF progression, in order to identify patients who would benefit from intensified treatment. Until recently, there has been little research evidence concerning how frequently VF tests should be carried out to optimally detect progression. It appears that the timetabling of VFs, in routine clinical practice, is often intermittent and not well planned. In 2008, Chauhan *et al.*, a group of leading experts in VFs and glaucoma research, published recommendations for measuring rates of VF loss in newly diagnosed glaucoma patients based on statistical power calculations (Chauhan BC, Garway-Heath DF, Goni FJ, Rossette L, Bengtsson B, Viswanathan AC, *et al.* Practical recommendations for measuring rates of visual field change in glaucoma. *Br J Ophthalmol* 2008;**92**:569–73. http://dx.doi.org/10.1136/bjo.2007.135012). Fundamental to their results was the key principle that an adequate number of VF tests must be performed over a given period in order to separate true disease progression from the measurement variability inherent

in VF data. This conclusion is equivalent to the accepted notion that a clinical trial will not be sufficiently powered to detect an experimental effect if too few patients are enlisted. One particular finding from the Chauhan *et al*. study suggested that newly diagnosed glaucoma patients should undergo VF testing three times per year in the first 2 years post diagnosis. This frequency of testing identifies rapidly progressing eyes with greater certainty than if annual testing was implemented; progression was defined as a loss of the mean deviation (MD) index, which measures overall VF defect severity of more than 2 dB per year. Consequently, this recommendation has been adopted in the European Glaucoma Society (EGS) guidelines on patient examination.

The purpose of this project was to explore the clinical effectiveness and cost-effectiveness of using different monitoring intervals to detect disease worsening or stability in patients diagnosed with glaucoma. These questions were investigated using existing NHS data from current practice and new research knowledge was provided through statistical and health economic modelling.

Objectives

1. To survey and establish the current use of VF resources and to determine current practice in terms of follow-up for a newly diagnosed patient in NHS glaucoma services in England.
2. To explore glaucoma patients' views on VF testing during the follow-up of their condition.
3. To explore glaucoma clinicians' views on frequency of VF testing for newly diagnosed glaucoma patients.
4. To retrospectively investigate the distribution of the rate of VF progression in a large cohort of patient records already archived from four different glaucoma clinics from hospitals in England. Information about rates of progression in representative groups of glaucoma patients under clinical care will help us to model typical results achieved with currently available treatment modalities and inform about the magnitude of current and projected future visual function deficits caused by glaucoma.
5. To further develop a model for generating 'virtual' series of VFs in order to explore different follow-up schemes. In particular, annual testing will be compared against three tests per year for clinical effectiveness in determining glaucomatous progression.
6. To refine an existing health economic model for glaucoma care to estimate the cost-effectiveness of proposed practice (the EGS recommendation of six VFs in the first 2 years) on long-term health outcomes.

Methods

Each of the six objectives listed above were investigated as follows:

1. To estimate current clinical practice for the frequency of VF monitoring, a cross-sectional review of all patients attending specialist glaucoma clinics at six hospitals in England was performed.
2. To explore patient views and experiences of glaucoma monitoring, particularly with regards to the type and frequency of VF testing, patient focus groups took place at three different eye hospitals in England.
3. To establish the attitudes of glaucoma subspecialists to the frequency of VF testing, a five-item questionnaire was administered to all UK glaucoma specialists as listed by the Royal College of Ophthalmologists ($n = 150$). Each participant was required to self-complete the questionnaire and return it to the experimenters anonymously.
4. To investigate the rate of VF progression in clinical populations, a retrospective multicentre study of VF databases from four separate hospitals was conducted, comprising 473,252 VFs in 88,954 patients.
5. To advance our model for simulating VFs, VF variability was estimated using the VF data described above; these data were used to build a non-parametric model to simulate VFs and characterise MD variability. We were then able to model the statistical effectiveness of different follow-up schemes.

6. In order to model and evaluate the economic consequences of different VF monitoring intervals for patients newly diagnosed with glaucoma, a review of literature regarding the costs, utility and treatment of the disease was undertaken to build a health economic model for glaucoma care.

Results

Investigating the six objectives listed above led to the following results:

1. The multicentre cross-sectional study demonstrated that no patients received the frequency of VF testing recommended by the EGS guidelines (six VFs in the first 2 years). Instead, patients typically had only two to three VF tests in the first 2 years following diagnosis, generally taking more than 4 years on average to reach six VFs.
2. Patient focus groups indicated that although patients did not like VF testing, they accepted it as an important part of their vision assessment and disease management. Interestingly, patients raised concerns regarding distracting testing environments, the quality of test instructions, explanation of results and excessive waiting times.
3. The results from the survey of glaucoma subspecialists suggested there is a large disparity in attitudes to setting follow-up intervals for glaucoma patients, with assigned intervals for VF testing that were often inconsistent with the guidelines from NICE. Furthermore, many specialists regard the research-recommended idea of six VF examinations in the first 2 years as not possible with current capacity.
4. The study of VF databases provided a number of interesting findings. In particular, only a small proportion of glaucoma patients progress at a rate faster than –2 dB/year. Moreover, older patients tend to progress more rapidly compared with younger patients, which is a key consideration when assessing visual impairment in a patient's expected lifetime.
5. Our computer model suggested that VF variability depends on the level of damage as well as the pattern of VF damage. Furthermore, proposed practice (six VF tests in the first 2 years) identifies progression sooner than current practice; however, the effectiveness of proposed practice over current practice (annual VF testing) is less beneficial than that suggested in the Chauhan *et al.* study for early identification of progression.
6. The health economic model of increased early VF monitoring suggested that this practice may be cost-effective [incremental cost-effectiveness ratio (ICER) was equal to £21,679], especially when gains to society (rather than solely the UK NHS gains) are accounted for.

Conclusions

When managing a newly diagnosed glaucoma patient, the clinician's goal is to preserve the patient's visual function during his or her lifetime. The risk of severe visual impairment depends on the stage of disease at presentation and the life expectancy, as well as the rate (speed) of visual deterioration. Patients in whom VF loss is progressing rapidly are in greater danger of going blind than patients with slow progression. Hence, the EGS, based on research by Chauhan *et al.* recommends that six VF tests be carried out in the first 2 years after diagnosis in all newly diagnosed glaucoma patients, since this monitoring programme will detect rapid progression more quickly than annual testing. However, the Chauhan *et al.* study did not consider effect of the duration of follow-up on the time to detect progression. For example, six examinations in 2 years are less powerful in detecting change than six examinations in 6 years, as the total amount of change will be much lower after 1 year than after 6 years. Thus, we conducted further simulations and calculated the time period required to detect various rates of MD change. Our results suggested that the previous model exaggerates the effectiveness of proposed practice to identify MD progression. Nonetheless, it was evident that, using our VF model, proposed practice identifies progression sooner than current practice. Therefore, there is a strong rationale for more frequent monitoring at diagnosis to detect rapidly progressing patients.

Importantly, results from our health economic model suggested that proposed practice is likely to be cost-effective (ICER was equal to £21,679). Nevertheless, many glaucoma clinicians consider increased surveillance of the VF would be impossible with current resources. In addition, patient focus groups raised significant concerns about patient–doctor communication, including the quality of VF test instructions, testing environment and explanation of results. Ensuring the confidence and co-operation of the patient should be at the centre of monitoring.

Recommendations for research (in order of priority)

1. Our results suggest that increased surveillance of the VF in monitoring the newly diagnosed glaucoma patient is likely to be clinically effective and cost-effective. Thus, this research supports the suggestion by NICE for a RCT of different monitoring intervals. Furthermore, our findings represent a significant step towards planning such a RCT and justifying the cost of it.
2. Patient focus groups suggested that glaucoma patients have several concerns about VF test conditions and instructions. Clearly these factors can influence the reliability of VF results, which in turn affects clinical decision-making. Therefore, patient involvement is important for not only addressing some or all of the perceived barriers highlighted in this study, but ultimately for driving further research into the most efficient strategies for VF monitoring. Research is now required to determine better VF testing for clinics.
3. Many glaucoma subspecialists do not follow EGS recommendations for VF testing, as summarised by one respondent, '*[the recommendations are] totally out of touch with what is possible in the current NHS clinics with such limited capacity*'. Thus, it appears that additional resources are required to achieve proposed practice. Research is now required to determine strategies to overcome capacity issues in NHS glaucoma services.
4. Guidelines for optimum frequency of testing do not incorporate level of VF damage at presentation. Prospective studies should examine the advantages of tailoring glaucoma monitoring to the needs of each patient, based on the risk of future loss of visual function. Our computer model for VFs demonstrates that VF variability increases as VF damage increases; prescriptions for the frequency of VF testing should, therefore, also be dependent on the patient's individual VF (level and pattern of damage), as it is more difficult to detect progression in patients with advanced disease. There may be significant service delivery advantages in monitoring patients with early or moderate VF loss less frequently than patients with severe VF damage.
5. Another strategy worth further investigation is the sensible idea of varying intervals between VF tests to optimise detection of progression. Clustering VF tests at the beginning and end of a predetermined observation period (the 'wait-and-see' approach) has been shown, albeit with statistical modelling only, to identify more patients with rapid VF progression and with fewer false positives than testing at uniform intervals. The idea of scheduling VF tests in this way is particularly applicable to clinical trials in which VF progression is the functional marker for glaucomatous change.

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