Colour vision testing for diabetic retinopathy

Colour vision testing for diabetic retinopathy: a systematic review of diagnostic accuracy and economic evaluation

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Executive summary

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Executive summary

Background

Diabetic retinopathy (DR) is caused by pathological changes in the blood vessels of the retina, which can lead to blindness.

All patients with diabetes mellitus (DM) are at risk of DR, and generally risk increases with duration of diabetes. Despite advances in the management of DM, visual impairment due to DR remains a significant complication, in terms of both its consequences for the functioning and quality of life of individual patients and its wider socioeconomic impacts. DR remains the commonest cause of blindness in the working age population.

The early stages of retinopathy are usually asymptomatic with respect to the quality of vision experienced by the patient. However, the changes observed in the early stages have been shown to be predictive of progression to sight-threatening proliferative retinopathy and maculopathy. Therefore, early identification and monitoring of retinopathy is crucial for successful management, and regular screening examinations for sight-threatening retinopathy are an essential part of effective diabetes care.

The existing DR screening programme is based on retinal photography, the performance of which is known to be dependent upon the experience of the examiners and the techniques used. The introduction of additional screening tests might improve performance but has significant cost implications.

Colour vision testing (CVT) may potentially provide a cost-effective tool for diagnosing DR as part of a battery of tests carried out by the National Screening Programme for Diabetic Retinopathy (NSPDR).

Objectives

This project had three main objectives. These were:

1. To report the findings of a systematic review to determine (1) the diagnostic performance of CVT options to identify and/or monitor the progression of DR, and (2) the preferences of patients in relation to incorporating CVT in the retinopathy screening programme.
2. To report the findings of a survey of the clinical leads and programme managers of the NSPDR to determine what tests are currently used in the detection and management of DR, over and above the requirements of the programme, as well as their views on future research priorities.
3. To review previous economic studies of DR screening with CVT and develop a cost-effectiveness model to evaluate the potential efficiency of incorporating CVT into the current DR screening programme.

Methods

A systematic review of the diagnostic performance of CVT and patient preferences towards CVT was carried out. Both published and unpublished literature were identified from systematic searches of electronic sources including MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA) database (from database inception to September 2008); hand searching; consultation with experts in the field; and the NSPDR.

Study selection, data extraction and quality assessment were undertaken by two reviewers independently. Studies were assessed for methodological quality using QUADAS (Quality for Assessing Diagnostic Accuracy Studies) and were combined in a structured narrative synthesis. Sensitivities and specificities were plotted in receiver operating characteristic space when appropriate.

A survey of NSPDR clinical leads and programme managers was carried out using an online survey that was emailed to 192 potential participants. The objective of the survey was to assess which

diagnostic tools are used routinely by the local centres over and above those specified by the NSPDR, as well as to assess the views of the clinical leads and programme managers on future research priorities.

We identified previous economic evaluations of CVT screening for DR by adapting the diagnostic accuracy search strategy by replacing diagnostic filter terms with economics filter terms. We expanded the electronic sources searched to include specialist economic evaluation databases.

Based on studies identified in the systematic review of diagnostic accuracy, we developed a decision tree and Markov model to estimate the incremental costs and effects of adding CVT to the current NSPDR using digital photography of the retina. Evidence on additional parameters, such as the incidence of DR in the screened population, costs of diagnosis and treatment, and the effectiveness of laser photocoagulation therapy, was collected through critical appraisal of the literature. We developed two models to evaluate cost per quality-adjusted life-year (QALY) in type 1 and type 2 diabetes.

Results

A total of 25 studies were located reporting on CVT, including 18 presenting 2×2 diagnostic accuracy data. The quality of studies and reporting was generally poor.

The automated or computerised CVTs reported variable sensitivities (63–97%) and specificities (71–95%). One study reported good diagnostic accuracy estimates for the combination of computerised CVT and retinal photography for detection of sight-threatening diabetic retinopathy, but this single study included very few cases of retinopathy in total. Results for the other types of CVT (pseudoisochromatic plates, anomaloscopes, and colour arrangement tests) were heterogeneous but largely inadequate for screening for DR; most performed little better than chance, having Youden indices (sensitivity + specificity – 100%) close to zero.

No studies were located that addressed patient preferences relating to colour vision screening for DR.

Retinal photography is universally employed as the primary method for retinal screening by centres responding to the survey of current practice; none used CVT. The most frequently cited preference for future research was the use of optical coherence tomography for the detection of clinically significant macular oedema.

Our search of the economic evaluation literature found no previous studies describing the cost and effects of any type of CVT.

As only one small study directly compared the diagnostic accuracy of CVT with that of retinal photography, the results of our economic model, based on that study, are imprecise. Furthermore, that study estimated a high sensitivity and specificity of CVT compared with the other 17 CVT studies in our review. Therefore, the results of our economic model should be treated cautiously until further evidence is available.

Our economic evaluation suggested that the addition of CVT to the current national screening programme could be cost-effective if it adequately increases sensitivity and is relatively inexpensive. The base-case analysis indicated that the cost per QALY gained is £6364 and £12,432 for type 1 and type 2 diabetes respectively. However, our probabilistic sensitivity analysis highlighted the substantial probability that CVT is not diagnostically accurate enough to be either an effective or a cost-effective addition to current screening methods. Better quality diagnostic accuracy studies directly comparing the incremental value of CVT in addition to retinal photography are needed before drawing conclusions on cost-effectiveness.

Discussion

Not all CVTs have been evaluated; those that have were generally not considered in the context of a retinal photography-based screening setting. There are insufficient data on any predictive/protective value of CVT. There is a lack of primary studies evaluating the efficiency of including CVT in DR screening.

Conclusions

Implications for service provision

- There is insufficient evidence to support the use of CVT alone, or in combination with retinal photography, as a method for screening for retinopathy in patients with diabetes. The

evidence that is available is limited in quantity and is of generally poor quality.
- Limited evidence on variations of the automated Sussex Gratings Machine, when combined with retinal photography, indicated some promise. However, this technology has not been independently evaluated and cost-effectiveness has not been proven. Probabilistic sensitivity analysis highlighted the substantial probability that CVT is not diagnostically accurate enough to be either an effective or cost-effective addition to current screening methods.

Suggested research priorities

- CVT was not identified as a research priority by survey respondents; around one-third of respondents considered optical coherence tomography to be a research priority.
- Any study carried out to resolve outstanding uncertainties would have to evaluate the addition of CVT to retinal photography and be prospective; generalisable to a screening population; independent of test developers; designed to account for lens yellowing, iris colour, macular pigment density and other clinical factors; and compliant with STARD reporting guidelines.
- Any future studies should consider the consequences of positive and negative tests in terms of subsequent treatment/prevention options, costs and participant outcomes.
- Activity-based cost analyses detailing the resource use of the various manual and automated CVT strategies are also necessary. These studies should estimate the capital and labour costs of implementing CVT in typical primary care trust diabetic populations.

Publication

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NIHR Health Technology Assessment programme

The Health Technology Assessment (HTA) programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA programme then commissions the research by competitive tender.

Second, the HTA programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer reviewed by a number of independent expert referees before publication in the widely read journal series *Health Technology Assessment*.

Criteria for inclusion in the HTA journal series

Reports are published in the HTA journal series if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this issue of the journal was commissioned by the HTA programme as project number 07/28/02. The contractual start date was in October 2007. The draft report began editorial review in October 2008 and was accepted for publication in May 2009. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

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