The measurement of intra-ocular pressure and the frequency of follow up in patients at risk of glaucoma

Introduction

The aim of the HTA programme is to ensure that high quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage, provide care in or develop policy for the NHS. Topics for research are identified and prioritised to meet the needs of the NHS. Health technology assessment forms a substantial portfolio of work within the National Institute for Health Research and each year about fifty new studies are commissioned to help answer questions of direct importance to the NHS. The studies include both primary research and evidence synthesis.

Question

What is the optimum frequency of monitoring patients identified as at risk of glaucoma due to slightly raised intraocular pressure and to what extent does this vary according to their risk characteristics?

1 **Technology:** Frequency of monitoring of intraocular pressure.
2 **Patient group:** Patients who have slightly raised intraocular pressure (IOP).
3 **Setting:** Hospital eye clinics or opticians.
4 **Design:** Primary research in several parts. The researchers will:
- Systematically identify and review existing risk prediction tools for the progression of raised IOP to glaucoma, including that described in Medeiros et al Arch Ophthalmol. 2005;123:1351-1360.
- Develop, populate and separately validate a new model of risk prediction for progression of raised IOP using data from a secondary analysis of existing individual patient data sets. A comparison of the best existing and the new model should be made.
- Based on the performance of the best available risk prediction tool, researchers should identify appropriate thresholds for initiating regular surveillance and model the effect of different frequencies of follow-up on treatment decisions and patient outcomes and ascertain the cost-effectiveness and cost utility of different frequencies of follow up.
- Make recommendations for future research in this area.

5 **Primary outcome:** A validated risk prediction tool and algorithm for management of patients with slightly raised intraocular pressure. Secondary outcomes: a review of current risk prediction tools with an assessment of their validity; the cost-effectiveness and cost utility of different frequencies of follow up in patient risk group(s).

Background to commissioning brief:

Raised intra-ocular pressure is a risk factor for the development of glaucoma. However, there is uncertainty about the costs and rationale for monitoring ocular hypertension, including the factors for measuring intra-ocular pressure that may affect measurements. Little is known about the day-to-day and week-to-week fluctuations in intraocular pressure of individual patients with slightly raised ocular pressure.

Primary research is needed consisting of 1) an evidence synthesis in the form of a systematic review and appraisal of current risk prediction tools for the development of glaucoma over time in people with slightly raised IOP, 2) a secondary analysis of existing individual patient data sets (such as hospital eye clinics / opticians) to develop and separately validate a new model of risk prediction for the progression of raised IOP to glaucoma, 3) using the best available risk prediction tool, develop and populate a model of the effect of different

frequencies of follow-up with different thresholds of initiation of regular surveillance on patient outcomes, cost-effectiveness and cost utility.

Notes to Applicants

For many of the questions posed by the HTA programme, a randomised controlled trial is likely to be the most appropriate method of providing an answer. However, there may be practical or ethical reasons why this might not be possible. Applicants proposing other research methods are invited to justify these choices.

Applicants are asked to:

1. Follow the Medical Research Council's Good Clinical Practice guidelines (http://www.mrc.ac.uk/pdf-ctg.pdf) when planning how studies, particularly RCTs, will be supervised. Further advice specific to each topic will be given by the HTA programme at full proposal and contract stages.

2. Note that trials involving medicinal products must comply with "The Medicines for Human Use (Clinical Trials) Regulations 2004". In the case of such trials, the DH expects the employing institution of the chief investigator to be nominated as the sponsor. Other institutions may wish to take on this responsibility or agree co-sponsorship with the employing institution. The DH is prepared to accept the nomination of multiple sponsors. Applicants who are asked to submit a full proposal will need to obtain confirmation of a sponsor(s) to complete their application. The DH reserve the right to withdraw from funding the project if they are not satisfied with the arrangements put in place to conduct the trial.

The MHRA (info@mhra.gsi.gov.uk, http://www.mhra.gov.uk) can provide guidance as to whether your trial would be covered by the regulations. The DH/MRC website (http://www.ct-toolkit.ac.uk/) also contains the latest information about Clinical Trials regulations and a helpful FAQ page.

Research networks

The HTA programme expects, where appropriate, that applicants will work with the relevant research network.

Making an application

If you wish to submit an outline proposal on this topic, complete the electronic application form and return it to the HTA Commissioning Manager at the National Coordinating Centre for Health Technology Assessment, Mailpoint 728 Boldrewood, University of Southampton, Southampton SO16 7PX by **8 August 2007.** Outline applications will be considered by the HTA Commissioning Board at its meeting in ***November 2007***. If they are acceptable, investigators will be given a minimum of eight weeks to submit a full proposal.

Applications received after 1300 hours on the due date will not be considered.

Please see GUIDANCE ON APPLICATIONS overleaf.

Guidance on applications

Required expertise

HTA is a multidisciplinary enterprise. It needs to draw on the expertise and knowledge of clinicians and of those trained in health service research methodologies such as health economics, medical statistics, study design and qualitative approaches. The HTA programme expects teams proposing randomised controlled trials to include input from an accredited clinical trials unit, or one with equivalent experience. Applicants are also expected to engage a qualified Trial Manager for appropriate projects. A commitment to team working must be shown and applicants may wish to consider a collaborative approach between several institutions

Public involvement in research

The HTA programme recognises the increasing active involvement of members of the public in research and would like to support research projects appropriately. The HTA programme encourages applicants to consider *how* the scientific quality, feasibility or practicality of their proposal *might* be improved by involving members of the public. Research teams wishing to involve members of the public should include in their application: the aims of active involvement in this project; a description of the members of the public (to be) involved; a description of the methods of involvement; and an appropriate budget. Applications that involve members of the public will not, for that reason alone, be favoured over proposals that do not but it is hoped that the involvement of members of the public will improve the quality of the application.

Outcomes

Wherever possible, the results of HTA should provide information about the effectiveness and cost-effectiveness of care provided in its usual clinical setting and for the diverse subjects who would be eligible for the interventions under study. The endpoints of interest will in most cases include disease specific measures, health related quality of life and costs (directly and indirectly related to patient management). Wherever possible, these measurements should be made by individuals who are unaware of the treatment allocation of the subjects they are assessing. We encourage applicants to involve users of health care in the preparation of their proposal, for instance in selecting patient-oriented outcomes. A period of follow up should be undertaken which is sufficient to ensure that a wider range of effects are identified other than those which are evident immediately after treatment. These factors should guide applicants in their choice of subjects, settings and measurements made.

Sample size

A formal estimate should be made of the number of subjects required to show important differences in the chosen primary outcome measure. Justification of this estimate will be expected in the application.

Communication

Communication of the results of research to decision makers in the NHS is central to the HTA Programme. Successful applicants will be required to submit a single final report for publication by the HTA programme. They are also required to seek peer-reviewed publication of their results elsewhere and may also be asked to support the NCCHTA in further efforts to ensure that results are readily available to all relevant parties in the NHS. Where findings demonstrate continuing uncertainty, these should be highlighted as areas for further research.

Timescale

There are no fixed limits on the duration of projects or funding and proposals should be tailored to fully address the problem (including long-term follow-up if necessary). Applicants should consider however that there is a pressing need within the NHS for this research, and so the duration of the research needs to be timely.

In evaluating diagnostic and imaging techniques, the emphasis of the HTA programme is to assess the effect on patient management and outcomes (particularly where changes in management can be shown to have patient benefits). Improvements in diagnostic accuracy, whilst relevant, are not the primary interest of this commissioned research programme. Applicants should justify where they consider improvements in diagnostic accuracy to be relevant to these objectives. Where there is poor evidence to link diagnostic improvements to patient benefits, part of the primary research may be to assess the effects of such changes on patient outcome.

An assessment should also be made of changes in other resources (particularly other subsequent therapies) used as a result of changes in diagnostic methods.