Frequency of follow-up for patients with intermediate grade colorectal adenomas

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 and work in the NHS. Questions are identified and prioritised to meet the needs of the NHS and its patients. Health technology assessment forms the largest portfolio of work in the NHS Research and Development Programme and each year about forty new studies are commissioned to help answer questions of direct importance to the NHS. The studies include primary and secondary research and cost about £10 million a year.

Question

- What is the optimum frequency of surveillance for people who have intermediate grade colorectal adenomas?

1 **Technology:** Surveillance of intermediate grade adenomas with colonoscopy or sigmoidoscopy.
2 **Patient group:** Those with intermediate grade adenomas identified during colonoscopic screening for colorectal cancer or other colonoscopic assessment.
3 **Setting:** Secondary care
4 **Control or comparator treatment:** Shorter versus longer surveillance intervals
5 **Design:** The HTA programme intends to commission research in two stages. The first stage should take the form of an observational study of existing high quality clinical databases.
The second stage, funding for which will be awarded to the same team dependent on certain criteria (see section 7 below), will be a randomised controlled trial of different surveillance intervals: probably the 3 yearly interval recommended by the BSG guidelines against a longer interval. Research should stratify in order to identify and explore the relative risks associated with the characteristics of the patient and tumour (histological or genetic). Researchers will also need to justify their classification of intermediate adenomas.
6 **Primary outcomes:** Benefits and risks to the patient including prevention of cancer, preventing further advanced adenomas, anxiety, morbidity and mortality; costs and cost-effectiveness; implications to the NHS.
7 **Additional information:** Applicants should submit a **Full Primary Research Proposal** for the stage one databases study (to include an outline proposal for the RCT as an appendix). This proposal should include suggested criteria against which the HTA programme could judge the value of later requesting a full proposal for the RCT. These criteria are likely to include, but not be limited to, the following: (a) the databases study has completed successfully; (b) its results identify plausible surveillance intervals to be assessed in an RCT. The successful applicants will be invited to submit a full proposal for the randomised trial at a later date, if the criteria are met. That full proposal will need to include formal analysis of the value of information associated with the RCT.

Summary of research need:

Bowel cancer is a common cause of deaths in the UK, with more than 30,000 new cases diagnosed each year. A UK pilot of colorectal screening is currently underway; screening will also identify individuals with adenomatous polyps and it is unclear what surveillance is required for those classed as having intermediate adenomas.

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The British Society of Gastroenterology (BSG) have developed a definition of intermediate adenomas but other classifications may be in use. The option of no surveillance is unlikely to be acceptable.

Primary research is required to establish the optimum management strategy for surveillance of these intermediate adenomas. This should take the form of a multicentre cohort study using existing national databases followed, if appropriate, by an RCT of different surveillance intervals.

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 (www.mrc.ac.uk/clinical_trials/ctg.html) 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 European Union Directive 2001/20/EC. For trials covered by the Directive the DH, with the HTA programme acting as their agent, is prepared, *in principle*, to be nominated as the sponsor. The responsibilities of the sponsor, as indicated by the directive, will then be agreed amongst the HTA programme, the host institution and the successful applicant. The DH reserve the right to withdrawn from the role of sponsor if they are not satisfied with the arrangements put in place to conduct the trial. Experience shows that some host institutions prefer to assume the role of sponsor for purposes of the EU Clinical Trials Directive [2001/20/EC]. This is consistent with their duties and responsibilities under the Research Governance Framework and the HTA programme would support this approach.

If you are not clear as to whether your trial is covered by the directive you should contact the MHRA (info@mhra.gsi.gov.uk) for help in this matter. Their website (http://medicines.mhra.gov.uk/ourwork/licensingmeds/types/clintrialdir.htm) contains the latest information about the EU Clinical Trials Directive [2001/20/EC] and a helpful FAQ page

Making an application

If you wish to submit a proposal on this topic, complete the electronic application form and return it to the Commissioning Manager at the National Coordinating Centre for Health Technology Assessment, Mailpoint 728 Boldrewood, University of Southampton, Southampton SO16 7PX by Wednesday *17 November 2004.* Applications will be reviewed by the HTA Commissioning Board at its meeting in February 2005.

Applications received after <u>1300 hours</u> on the due date will not be considered.

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. HTA expects applicants to engage a qualified Trial Manager for appropriate projects. Applicants will need to show a commitment to team working and may wish to consider a collaborative approach between several institutions. It is expected that the research will be undertaken only following a thorough literature review.

Consumer involvement in research
The HTA programme recognises the increasing active involvement of consumers 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 consumers. Research teams wishing to involve consumers should include in their application: the aims of active involvement in this project; a description of the consumers (to be) involved; a description of the methods of involvement; a budget for consumer involvement. Applications that involve consumers will not, for that reason alone, be favoured over proposals that do not but it is hoped that the involvement of consumers 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 consumers 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. However, there is a pressing need within the NHS for the information and so the research would normally be expected to be completed within three years, unless long-term follow-up is necessary.