What is the best rapid test for streptococcal sore throat and does testing affect outcome in primary care?

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 effectiveness and cost-effectiveness of the use of rapid antigen detection test kits on the management and outcomes of patients presenting with sore throat in primary care?

1 **Technology:** Rapid antigen detection tests (RADTs) for group A streptococcus throat.
2 **Patient group:** Adults and children presenting with sore throat. Researchers may consider stratification by GP's degree of uncertainty about the cause / nature of sore throat.
3 **Setting:** Primary care.
4 **Design:** Research is required in two stages: a) A diagnostic test evaluation is required to assess the diagnostic performance of all currently marketed RADTs; b) Primary research of the best RADT identified in stage a) is required in the form of a randomised controlled trial.
5 **Control or comparator treatment:** a) Other RADTs b) Two controls for the RCT should be considered: empiric treatment (such as antibiotics for those who are unwell and delayed prescription for those who are more well); and treatment guided by use of a validated clinical rule, such as Centor.
6 **Primary outcomes:** a) Diagnostic performance of available tests in terms of sensitivity and specificity. b) Number of days ill; severity of symptoms; antibiotic use; recurrence; costs and cost-effectiveness. The medicalisation of illness (belief in the importance of seeing the doctor, reattendance) also needs to be considered.
7 **Minimum duration of follow-up:** 3 months for recurrence, up to 1 year for medicalisation.

Summary of research need:

Attendance in primary care for sore throat is high. In many patients the symptoms resolve without intervention, although in some the cause is bacterial and may benefit from antibiotics. Rarely, longer term, more serious, complications occur, such as rheumatic fever.

Currently the only recommended way to confirm that sore throat is bacterial is to take a swab and send it for laboratory analysis. Rapid near-to-patient tests may speed up diagnosis so that treatment can be more appropriately targeted. It is not known how accurate or useful rapid tests are in a primary care setting.

Research in two stages is therefore required: first, to assess diagnostic performance of all currently marketed rapid antigen detection tests against predefined success criteria; secondly, to evaluate the most effective of these tests in the management of patients with sore throat in primary care.

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 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 withdraw 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 an outline 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 27 April 2005.** Outline applications will be considered by the HTA Commissioning Board at its meeting in July 2005. 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.

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.

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 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.

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.