Duration of protection of BCG vaccine – updated systematic review and meta-analysis

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 current evidence on the duration of protection of BCG vaccine? (updated systematic review and meta-analysis)

1 **Technology*:*** Bacillus Calmette-Guerin (BCG) vaccine.
2 **Patient group:** People at risk of developing Tuberculosis.
3 **Setting:** Primary care.
4 **Control or comparator treatment:** No immunisation.
5 **Design:** A systematic review with meta-analysis of relevant randomised controlled trials, cohort studies and case-controlled studies. Researcher to consider, where possible and applicable, stratifying analyses by age, age at vaccination, gender and other demographic characteristics (researcher to justify).
6 **Outcomes:** Protective efficacy of BCG vaccination against tuberculosis by time since vaccination.
7 **Is the research question concerned with a licensed or unlicensed indication for the drug in question?** Licensed.

Background to commissioning brief:

Tuberculosis (TB) is an infectious bacterial disease which most commonly affects the lungs. The BCG (Bacillus Calmette-Guerin) vaccine has been used to prevent TB since 1953. In the UK, the BCG vaccine was routinely given to all schoolchildren until autumn 2005. Since autumn 2005 a 'risk based' programme has been in place which provides BCG vaccination for people at increased risk of getting TB, including in some areas newborn babies.

In 1993, the World Health Organization declared TB a global public health emergency. In 2000, 8.3 million new cases were reported, and an estimated 1.7 million people die of TB each year. Since 1987, new reported cases in England and Wales rose by nearly 40% to around 7000 in 2004 and there are still around 350 deaths each year either directly due to or associated with TB. Treating TB has become more difficult because many people are infected with drug-resistant organisms or have immune systems too weak to fight the infection.

It is not known how long the protection afforded by BCG lasts, particularly in different age and population groups, and this hinders the development of evidence-based policies about re-immunisation. A number of previous systematic reviews have addressed similar questions (Colditz 1995, Sterne 1998 and Trunz 2006) but there have been new primary studies published since. Because of this, and because there is a lack of evidence of protective efficacy in adult life, new research in the form of a systematic review is needed on the duration of protection from BCG vaccination for preventing TB.

Making an application

If you wish to submit a proposal on this topic, complete the electronic application form and return it, along with a detailed project description, to the HTA Commissioning Manager at the National Coordinating Centre for Health Technology Assessment, Mailpoint 728, Boldrewood, University of Southampton, Southampton SO16 7PX by **23 April 2008**.

Your full proposal will be assessed by designated Commissioning Board members, alongside other applications submitted in the same topic area. They will decide on a maximum of three proposals to be taken forward for peer review by external referees, and subsequent consideration by the HTA Commissioning Board at its meeting in **July 2008.**

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

Please see GUIDANCE ON APPLICATIONS overleaf.

Guidance on applications

Methods
Applicants should demonstrate knowledge of current research in the field and of systematic review methods and state how these would apply to the question posed. Valid and reliable methods should be proposed for identifying and selecting relevant material, assessing its quality and synthesising the results. Guidance on choice of appropriate methods is contained in NHS CRD Report 4 *Undertaking systematic reviews of research on effectiveness* (www.york.ac.uk/inst/crd/report4.htm). Where policy implications are considered, the emphasis should be on assessing the likely effects of a range of policy options open to decision makers rather than a judgement on any single strategy. Where epidemiological modelling or economic evaluation is required, the range of uncertainty associated with the results should be assessed. In the assessment of cost-effectiveness, further data collection may be required to estimate resource use and costs. If there is evidence that the ratio of costs and benefits may differ between readily identifiable groups, applicants are encouraged to state how they will identify these differences.

Cochrane
Applicants wishing to produce and maintain a Cochrane systematic review from this HTA commissioned systematic review should make the case in their proposal. This will need to include the approval of the relevant Cochrane Review Group (www.cochrane.org). Any additional costs associated with the initial preparation of a Cochrane review should be included in your project proposal. Maintenance costs cannot be met.

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.

Updating
It is the policy of the NCCHTA that all search strategies undertaken as part of evidence synthesis/secondary research projects must not be more than 12 months out of date when the draft final report is submitted. We expect that most projects will manage to bring their searches up to date prior to analysis and writing up. As research funders we are aware that exceptional circumstances can apply that would not allow this to be case but this must be the exception rather than the rule and will be assessed on a case by case basis. The expectation is that projects funded by the HTA programme will deliver information that is both relevant and timely.

In addition, in order to inform decisions on whether and when to update the review, researchers will be expected to give some indication of how fast the evidence base is changing in the field concerned, based on the nature and volume of ongoing work known at the time the review is completed. Applicants should note that they will not be expected to carry out any future updating as part of the contract to complete the review.

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 communicate their work through peer-reviewed journals 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. However, there is a pressing need within the NHS for the information and so the research would normally be expected to be completed as soon as possible – however it is for applicants to justify the duration and costs proposed.