Responding to a small-scale bioterrorist anthrax attack: cost-effectiveness analysis comparing preattack vaccination with postattack antibiotic treatment and vaccination


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study compared three strategies for the management of a small-scale anthrax attack.

Strategy 1 was pre-attack vaccination of all US distribution centre postal workers using cell-free anthrax vaccine administered in 6 doses at day 1, at 2 and 4 weeks, and at 6, 12 and 18 months, respectively.

Strategy 2 was post-attack antibiotic therapy (ciprofloxacin) for exposed employees for 60 days followed by vaccination (3 doses of vaccine at 1, 14 and 28 days, respectively).

Strategy 3 was post-attack antibiotic therapy (ciprofloxacin) for exposed employees for 60 days without vaccination.

Type of intervention
Prevention and treatment.

Economic study type
Cost-utility analysis.

Study population
As this was a modelling study, the target population comprised a cohort of 350,000 postal service employees aged between 18 and 60 years who had not been exposed to anthrax before. Delivery carriers, motor vehicle operators and maintenance personnel were excluded from the study. The workforce turnover was assumed to be 10% annually.

Setting
The setting was secondary care and the community. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness parameters use to populate the model came from studies published between 1954 and 2004. The price year was 2005. Estimates about resources used were based on a study published in 2002.

Source of effectiveness data
The following clinical parameters were included in the model:

the annual probability of an anthrax attack,

the probability of exposure and percentage of inhalation anthrax in exposure, and

the probability of inoculation after exposure.
The probabilities of adverse events of oral antibiotic treatment and anthrax vaccination, and the probability of death due to anthrax inhalation without and after hospitalisation, were also obtained.

**Modelling**
A Markov model with a 10-year time horizon was developed to estimate the cost-effectiveness of the three strategies and their impact on morbidity and mortality. The health states and transition probabilities were all reported. Modelling assumptions were reported and fully justified.

**Sources searched to identify primary studies**
The probability of an attack was based on researchers’ assumptions, while baseline probabilities, effectiveness and data on adverse events were derived from published studies. However, the designs of the clinical studies were unclear.

**Methods used to judge relevance and validity, and for extracting data**
The process used to identify the data was not reported. No inclusion criteria for any parameters were specified. In addition, there was no discussion of method used to estimate probabilities where no published estimates were available.

**Measure of benefits used in the economic analysis**
The measure of benefit used was the quality-adjusted life-years (QALYs). Quality of life weights were derived from published studies reporting utilities for similar health states. Short- and long-term adjustments performed by the authors were reported in full. The benefits were discounted at a rate of 3%.

**Direct costs**
The study reported the direct costs to the health service. These were the costs of the vaccine and its administration, antibiotic therapy, adverse events due to vaccination, oral and cutaneous treatment, and the cost of dying due to anthrax (including hospitalisation). The costs and resource use were derived from official sources and a published study (Inglesby et al. 2002, see ‘Other Publications of Related Interest’ below for bibliographic details) and were reported in full. The costs were reported as the average cost per patient. The costs were adjusted for inflation using the Consumer Price Index and were discounted at an annual rate of 3%. The price year was 2005.

**Statistical analysis of costs**
The cost data were treated deterministically.

**Indirect Costs**
Productivity costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were conducted for all variables in the model. The ranges used were reported in full and were mainly derived from published literature. Two-way analyses were conducted to investigate varying adherence and response time, assuming 1% and 10% inoculation rates, respectively. Separate sensitivity analyses were performed for the assumptions of a 4-month duration of antibiotic therapy and the administration of post-attack prophylaxis within the first 12 hours after exposure. A threshold analysis was also conducted to estimate the minimal improvement in effectiveness gained due to the addition of post-attack vaccination such that the combined strategy of post-attack antibiotic therapy and vaccination remains cost-effective. A willingness-to-pay threshold of $100,000 was applied.
Separate sensitivity analyses were performed to investigate the scenarios of a mass vaccination of postal workers before an attack, and the effect of assuming a positive probability of attack but zero probability of adverse reaction to vaccination, slow attack response, no adherence to post-attack antibiotic therapy, and complete adherence to vaccination.

Monte Carlo simulations on 1,000 randomly selected observations were conducted to investigate the robustness of the results to the entire range of possible parameter values. Thirty-six variables were varied simultaneously using different scenarios for infectious dose, response time and adherence to prophylactic treatment. Distributions were reported. Dominated strategies (with higher incremental cost-effectiveness ratios, ICERs) were excluded from the Monte Carlo simulations.

**Estimated benefits used in the economic analysis**
The strategy of post-attack antibiotic therapy alone resulted in 14,801,486.23 QALYs.

The strategy of post-attack antibiotic therapy combined with vaccination resulted in 14,801,492.71 QALYs.

The pre-attack vaccination strategy resulted in 14,801,456 QALYs.

**Cost results**
The strategy of post-attack antibiotic therapy alone resulted in a cost of $1,568,455.59.

The strategy of post-attack antibiotic therapy combined with vaccination resulted in a cost of $1,954,188.18.

The pre-attack vaccination strategy resulted in a cost of $105,617,002.

**Synthesis of costs and benefits**
An incremental cost-effectiveness analysis was performed. This demonstrated that the combined post-attack antibiotic therapy and vaccination strategy was the most cost-effective strategy, resulting in an ICER of $59,558 per QALY in comparison with post-attack antibiotic therapy alone. The pre-attack vaccination strategy was dominated, which means it was more costly and less effective than a comparator.

The sensitivity analyses demonstrated that post-attack antibiotic therapy alone became the preferred strategy when the death rate due to anthrax was lower than 1.4%.

Pre-attack vaccination resulted in an ICER of less than $100,000 per QALY compared with post-attack antibiotic therapy alone only with complete adherence to pre-attack vaccination and a probability of exposure of at least 18.5%.

Monte Carlo simulations conducted for the scenario of a 10% infectious dose, complete adherence and slow response time only compared pre-attack vaccination with post-attack antibiotic therapy. It was demonstrated that post-attack antibiotic therapy was cost-effective when 100% adherence to antibiotic therapy was assumed, the response time was rapid, and the inoculation rate was 10%.

**Authors' conclusions**
Post-attack antibiotic therapy combined with the vaccination of exposed personnel is the most favourable strategy to manage an anthrax attack conducted through the US Postal Service.

**CRD COMMENTARY - Selection of comparators**
A justification was provided for the technologies compared. All had been recommended in published literature as possible public health strategies for anthrax attacks. You should decide if these represent valid comparators in your own setting.
Validity of estimate of measure of effectiveness
The parameters of the model were mainly derived from published literature. No systematic search for data was reported. Data from available studies appear to have been used selectively. It is not possible to judge the validity of the evidence used to derive estimates given the limited information reported in the current study.

Validity of estimate of measure of benefit
The estimation of health benefits (QALYs) was modelled using a Markov model. The utility weights were derived from published studies, and all the adjustments the authors made were reported in full. The QALYs were appropriately discounted.

Validity of estimate of costs
The authors reported that the study had been conducted from a societal perspective, but productivity costs were not included. Disposable costs of vaccination were excluded from the analysis, but their omission is unlikely to have affected the authors' conclusions. Adjustments for inflation, discounting and the price year were appropriately reported. An extensive sensitivity analysis of the costs was conducted to assess the robustness of the estimates used, thus enhancing the generalisability of the results to other settings.

Other issues
The authors did not compare their findings with those from other studies, so it is not possible to determine to what extent their results agree with other published results. The issue of the generalisability of the results to other settings was not directly addressed, but extensive sensitivity analyses will have improved the external validity of the study. The authors' conclusions would appear to be an adequate reflection of the scope of the analysis. The authors reported two limitations to their study. First, that antibiotic treatment duration at baseline was considered to be short, although variation of treatment duration did not alter the authors' conclusions. Second, although the study was limited to a small-scale attack, there is a risk of a large-scale attack in the USA. Extrapolation of the analysis for a large-scale attack demonstrated that the optimal option remains the same; only the results of the sensitivity analyses differed.

Implications of the study
The authors stressed the importance of developing a plan for rapid delivery of post-attack vaccination and treatment to successfully counter future attacks. Recommendations for future research were not provided, although the discussion highlighted areas where more robust information is necessary.

Source of funding
Supported by a grant from the Department of Veterans Affairs.

Bibliographic details

PubMedID
17420423

DOI
10.1001/archinte.167.7.655

Other publications of related interest
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the
abstract and their bibliographic details recorded here for information.


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Anthrax /drug therapy /prevention & control; Anthrax Vaccines /economics; Anti-Bacterial Agents /economics /therapeutic use; Bioterrorism; Cost-Benefit Analysis; Emergency Medical Services /economics; Humans

**AccessionNumber**
22007008087

**Date bibliographic record published**
31/10/2007

**Date abstract record published**
31/10/2007