The cost-effectiveness of strategies to reduce mortality from an intentional release of aerosolized anthrax spores

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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 assessed mitigation strategies aimed at reducing mortality and morbidity from intentional exposures to aerosolised anthrax. The authors looked at a universal vaccination strategy and an emergency surveillance and response (ESR) system. The ESR system was assumed to comprise two separate constituent systems. The first was a surveillance system designed to detect anthrax exposure more rapidly, that is, immediately after the first person seeks medical treatment for fulminant-stage inhalational anthrax. The second was a response system designed to administer post-exposure prophylaxis more rapidly by increasing the dispensation capacity ten-fold compared with baseline.

Type of intervention
Primary prevention, diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The hypothetical study population comprised residents of large US metropolitan areas.

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

Dates to which data relate
The effectiveness data referred to 1960 to 2004. The resource use and cost data referred to 1999 to 2001. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a review of published studies, and also authors' and expert opinion.

Modelling
A Markov model was used to simulate the effects of an uncertain intentional exposure to inhalational anthrax and to estimate the cost-effectiveness of the alternative mitigation strategies. The health states in the model were unexposed, exposed, asymptomatic infection, prodromal infection, fulminant infection, recovered and dead. The time horizon for the model was 1 year.

The model considered two scenarios of surreptitious exposure. One scenario was a 100,000-person single-source exposure, similar to the worst-case scenario in previous analyses. The other scenario was a 100-person multiple-source exposure, similar to the recent US exposures.
The model assumed that the anthrax vaccination series was offered universally to all metropolitan-area residents before any exposure occurred, and that completion of this regimen would decrease the likelihood of infection among exposed persons. The model also assumed that the time taken to identify the cause of death would be 2 days in the base-case analysis.

Outcomes assessed in the review
The outcomes assessed in the review included:

- time course of disease and symptom progression,
- vaccine efficacy,
- vaccine toxicity,
- mortality from adverse events,
- compliance with vaccination, and
- the efficacy of and adherence with post-exposure prophylaxis.

Study designs and other criteria for inclusion in the review
The authors did not state that a systematic review was undertaken. They also did not describe the study designs or criteria for inclusion in the review.

Sources searched to identify primary studies
The authors did not state the sources searched to identify primary studies.

Criteria used to ensure the validity of primary studies
The authors did not describe criteria used to ensure the validity of the primary studies, but in many cases they used the most recent data.

Methods used to judge relevance and validity, and for extracting data
The authors did not describe the methods used to extract data from the primary studies. In many cases the studies were used to inform authors' assumptions.

Number of primary studies included
The review included at least 23 primary studies.

Methods of combining primary studies
Data from the primary studies were combined using a narrative method.

Investigation of differences between primary studies
The authors did not report any investigation into the differences between the primary studies.

Results of the review
The probability of developing prodromal symptoms if infected was 0.11 (range: 0.05 to 0.5). The probability of developing fulminant symptoms following prodromal symptoms was 0.23 (range: 0.1 to 1.0).
The daily probability of dying with fulminant symptoms was 0.29 (range: 0.1 to 1.0).

Compliance with vaccination was 0.22 (range: 0.1 to 0.9), and vaccine efficacy was 0.92 (range: 0.1 to 1.0).

The mortality due to adverse events from anthrax vaccination was 0.000001 (range: 0.00001 to 0.0000001).

The efficacy of treatment was 0.55 (range: 0.14 to 0.94).

Adherence with post-exposure prophylaxis for the 100-person exposure scenario was 0.44 (range: 0.40 to 0.60).

**Methods used to derive estimates of effectiveness**
The estimates of the performance abilities of an ESR system were derived from public health experts based in Pittsburgh and New York City. In the absence of data, the authors made assumptions about the values of several model parameters.

**Estimates of effectiveness and key assumptions**
It was assumed that the sensitivity of the surveillance system was 1 and that of the response system was 0.95 (range: 0.5 to 1.0), and that the specificities were 0.1 (range: 0.01 to 1.0) and 0.1 (range: 0.002 to 1.0), respectively. The probability of infection if exposed was assumed to be 0.5 (range: 0.1 to 0.9). The efficacy of post-exposure prophylaxis was assumed to be 0.80 (range: 0.25 to 1.00). Adherence to post-exposure prophylaxis following the 100,000-person exposure scenario was assumed to be 0.90 (range: 0.80 to 1.00).

**Measure of benefits used in the economic analysis**
The measure of benefit used was the life-years saved (LYS) over the 1-year time horizon. The LYS were derived directly from the model.

**Direct costs**
The study reported the costs but not resource use quantities. The study included direct costs to the health service and other agencies involved in operating an ESR system and responding to an intentional exposure to inhalational anthrax. These included the costs of purchasing and administering the vaccine, the fixed and variable costs of administering an ESR system, and the costs of drugs, outpatient and inpatient care for inhalational anthrax. Vaccine costs were based on military procurement expenses and drug costs on published pricing lists. The costs of the ESR system were derived using expert opinion. The costs of inpatient and outpatient care were derived from published studies. Discounting was not relevant given the 1-year time horizon. The study reported the average costs. All cost estimates were inflated to 2002 using the Consumer Price Index.

**Statistical analysis of costs**
Individual patient level data were not available, so a statistical analysis of the quantities and costs was not possible.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis of most parameters included in the model was conducted. This investigated variability in the data...
and uncertainty around modelling assumptions. Both one-way sensitivity analyses and a full probabilistic sensitivity analysis were undertaken. The probabilistic analysis was undertaken using 10,000 Monte Carlo simulations and the uncertainty around model parameters was characterised using uniform distributions.

**Estimated benefits used in the economic analysis**
With no mitigation strategy, 39.48653 life-years would be saved for a certain anthrax attack resulting in a 100,000-person exposure, increasing to more than 39.49999 LYS for a certain anthrax attack resulting in a 100-person exposure. For an unlikely attack with 0.001 probability, the number of LYS with no mitigation strategy was 39.49998 for a 100,000-person exposure and more than 39.49999 for a 100-person exposure.

With vaccination, the number of LYS following a certain attack was 39.38945 for a 100,000-person exposure and 39.49999 for a 100-person exposure. For an uncertain attack with a probability of 0.001, these figures were 39.49998 (100,000-person) and 39.49999 (100-person), respectively.

With an ESR system, the number of LYS following a certain attack was 39.49358 for a 100,000-person exposure and more than 39.49999 for a 100-person exposure. For an uncertain attack with a probability of 0.001, these figures were 39.49999 (100,000-person) and more than 39.49999 (100-person), respectively.

These health outcomes were estimated over a time horizon of 1 year and included mortality due to side effects from treatment.

**Cost results**
The cost per person of no mitigation strategy was $1.15 for a certain attack resulting in a 100,000-person exposure and less than $0.01 for the other scenarios.

The cost per person of universal vaccination was $83.44 for a certain attack resulting in a 100,000 person exposure and $82.56 for the other scenarios.

The cost per person of an ESR system was $1.66 for a certain attack resulting in a 100,000 person exposure and $1.01 for the other scenarios.

These costs were estimated over a time horizon of 1 year.

**Synthesis of costs and benefits**
The costs and benefits were synthesised to calculate the cost per LYS.

For a certain 100,000-person exposure, a vaccination strategy was estimated to cost $29,580 per LYS compared with no mitigation strategy. For all other scenarios, it was dominated by no mitigation strategy.

The cost per LYS with an ESR system compared with no mitigation strategy was estimated to be $73.00 in the case of a certain attack leading to a 100,000-person exposure, rising to $1,680,000 for a 100-person exposure. For an uncertain attack with probability 0.001, these estimates were $142,300 (100,000-person) and more than $1 billion (100-person), respectively.

The results were sensitive to variations in a number of parameters. For a certain attack that resulted in a 100,000-person exposure, the probabilistic analysis indicated that vaccination had 86.4% probability of having a cost per LYS of less than the commonly used threshold of $50,000. An ESR system was estimated to have a cost per LYS of less than $50,000 in 99.6% of simulations.

**Authors’ conclusions**
A mitigation strategy would only be cost-effective if there was a high probability of an attack that would result in a large exposure.
CRD COMMENTARY - Selection of comparators
The authors focused on a vaccination strategy and ESR system, but indicated that the model developed could be used to assess the cost-effectiveness of many other possible mitigation strategies. The analysis was based on the capacity constraints and typical services of the US health care system, thus the baseline of no mitigation strategy may not be generalisable to other countries with different health care systems and capacity constraints. You should consider whether the comparators presented here are relevant in your own setting.

Validity of estimate of measure of effectiveness
The estimates of effectiveness were derived from published studies, supplemented by authors' and expert opinion. The authors did not state that a systematic review of the literature had been undertaken. They made selective use of the available data in a modelling study. The estimates of effectiveness were combined using a narrative method. The authors justified their assumptions with reference to published studies. Expert opinion was obtained from discussion with experts. The authors acknowledged that the use of incomplete and subjective information was a limitation of the study.

Validity of estimate of measure of benefit
The estimation of health benefits was modelled over a period of 1 year. The cohort model used was appropriate given the authors' assumptions.

Validity of estimate of costs
The authors did not specify a perspective for the analysis. Since the study did not include the indirect costs, the perspective was not that of society. However, the perspective adopted was wider than the health service as it included the administration of an ESR system. The costs and the quantities were not reported separately, thus making it difficult to reproduce the study in other settings. The costs of an ESR system were based on expert opinion and are likely to be specific to the USA; the use of military procurement expenses was also likely to be specific to the USA. Uncertainty in the cost data was explored in sensitivity analyses, using wide ranges to reflect high levels of uncertainty given the lack of data around many parameters. The use of uniform distributions implies that any value within the plausible range is considered equally likely. The price year was reported, and the medical and non-medical costs were inflated to 2002 appropriately using the Consumer Price Index. The authors acknowledged that a 1-year time horizon was unfavourable towards a vaccination strategy as the costs of this strategy occur disproportionately in the first year. However, the authors stated that their underestimate of the cost-effectiveness of the vaccination strategy should not affect the study results.

Other issues
The authors made appropriate comparisons of their findings with those from other studies and attempted to explain any differences. The issue of generalisability to other settings was not directly addressed. The authors do not appear to have presented their results selectively and their conclusions reflected the scope and the limitations of the analysis.

Implications of the study
The authors did not make explicit recommendations for changes in policy or practice, nor did they suggest areas for further research. However, the discussion highlighted areas where more research information is needed.

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