Cost effectiveness of rabies post exposure prophylaxis in the United States
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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.

CRD summary
This study evaluated the cost-effectiveness of treatment to prevent rabies after exposure, in several transmission scenarios. The authors concluded that prophylaxis after bat bite exposure might be cost saving, but the uncertainty surrounding the transmission rates prevented firm conclusions. The study was clearly reported. There were some key limitations to the methods, including highly uncertain rabies transmission parameters and a crude valuation of human life. The authors’ conclusions should be used with caution.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study evaluated the cost-effectiveness of preventive treatment after exposure to rabies, given several transmission scenarios.

Interventions
Preventive treatment was compared with no treatment, in seven transmission scenarios: dog bite, dog lick, cat bite, cat lick, bat bite, rabid animal (skunk) bite, and exposure to a person with rabies. Treatment was five doses of human diploid cell vaccine, and one 6.3mL dose of human rabies immunoglobulin.

Location/setting
USA/public health.

Methods
Analytical approach:
An economic model was developed to assess the cost-effectiveness of rabies prevention over one year. The analysis focused on determining the probability of exposure that was cost saving, when the value of a human life was measured by future earnings. The authors stated that they took a societal perspective.

Effectiveness data:
The key measures of effectiveness were the prophylaxis efficacy and the probability of transmission, in each of the seven scenarios. The authors assumed that treatment was 100% effective in preventing rabies (no deaths). Without treatment, the outcome was assumed to be certain death. The probability of rabies, from a bite from an animal that was confirmed to have rabies, was from a range of death rates for different severity of exposure, from a 1912 book; these values were similar to those from more recent World Health Organization studies. Where the animal was not available for testing, a range of probabilities of transmission was used, based on the opinion and consensus of a 20-member panel, with a median experience of 1,700 rabies consultations per member.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The benefits were measured by the lives saved with prophylaxis.

Cost data:
The cost categories included biologic drugs, hospital care, indirect patient costs, and the monetary value of a human life.
life. The costs and resource use for the biologic vaccine and human rabies immunoglobulin were from a published study. The hospital costs were from the same study, and included emergency room visits and physician charges. Indirect patient costs included travel, lost wages, alternative medicines and other costs. These were from a published US retrospective study. The monetary value of a human life was their estimated future earnings and housekeeping services, based on a published textbook method, with age weighting. All costs were in 2004 US $. Biologic and hospital costs were inflated using the medical care consumer price index. Indirect costs and life values were inflated using government price indices. The value of a human life was discounted at 3% annually, with an estimated 75-year lifespan.

Analysis of uncertainty:
The cost of prophylaxis, and the value of a human life, were doubled in sensitivity analyses. For each transmission scenario, for the main analysis and doubled sensitivity analyses, the minimum cost-effectiveness per life saved ratios were calculated, using maximum transmission probabilities and minimum costs for treatment; the opposite values were used to calculate the maximum cost-effectiveness ratios.

Results
In the main analysis, the cost of prophylaxis was $4,042, the value of a human life was $1,109,920, and the transmission rate at which treatment was cost-saving was 0.36%. If the risk of rabies transmission was above 0.7%, prophylaxis was cost saving, in all scenarios.

In all cost scenarios, prophylaxis for bites from animals confirmed to have rabies was cost saving. On average, prophylaxis for bites from species known to have rabies, such as skunks, was cost saving. The average cost per life saved varied from $2.9 million to $4 billion.

When assessing extreme values, treatment for bat bites and cat bites could be cost saving, at high transmission probabilities and low costs. With low transmission probabilities and high costs, treatment for any exposures to animals without confirmed rabies, had a cost per life saved greater than $840 million, and usually closer to $8.4 billion.

The cost savings for treatment for bites from animals confirmed to have rabies or skunks were robust in the sensitivity analyses.

Authors' conclusions
The authors concluded that if the risk of rabies transmission was above 0.7%, prophylaxis was cost saving, and it was likely that prophylaxis after bat bite exposure could be cost saving, but the uncertainty surrounding the transmission rates was too great to reach firm conclusions.

CRD commentary
Interventions:
The interventions were clearly described. It was not clear if no treatment was an appropriate comparator. The prophylaxis protocol was based on a published study, and validated on a health care database.

Effectiveness/benefits:
The transmission probabilities for bites from animals with confirmed rabies were clearly described, but they were from a 1912 French publication, rather than more recent World Health Organization publications. The values from these more recent publications were not reported. How the source was identified and chosen was not reported, so it is unclear if the best available evidence was used. The remaining transmission probabilities, for potential rabies cases, were derived by Delphi panel, but the number of rounds of agreement and the methods for surveying the panel were not reported. The agreed average and minimum and maximum values were reported. Where effectiveness assumptions were made, the limitations of these assumptions were acknowledged.

Costs:
The costs were clearly reported, with clear methods, valid inflation methods, and justified assumptions. The value of a human life accounted for lost future wages and housework of the deceased, which was a very limited perspective of the value of life. It should also include the value of future health. The authors acknowledged this limitation, but the sensitivity analysis doubling the value of a life was arbitrary, and did not provide any insight into the range of alternative values. The evaluation of the willingness to pay for an additional life might have been more appropriate. It
was unclear at what age rabies exposure was assumed to occur, making the effect of discounting unclear.

Analysis and results:
Cost-effectiveness was calculated as the cost of prophylaxis, minus the probability of death without treatment multiplied by the value of a life, divided by the probability of death without treatment multiplied by the value of a life. Where this cost per life saved was negative, prophylaxis was considered to be cost saving. This method and the sensitivity analysis were clearly presented, but the authors acknowledged that they were limited in their ability to provide conclusive results. The sensitivity analyses used extreme values, but did not assess the distribution of different values. No variance statistics were reported, which makes it difficult to evaluate uncertainty. The analysis focused on whether treatment was cost saving – the threshold at which the costs might be considered acceptable was not analysed, which limits the applicability of the analysis. The authors highlighted the limitations to their study. Some of the uncertainty could have been assessed, using Monte Carlo simulation, to give an indication of how likely it was that treatment would be cost saving.

Concluding remarks:
The study was clearly reported. There were some key limitations to the methods, including highly uncertain rabies transmission parameters and a crude valuation of human life. The authors’ conclusions should be used with caution.

Funding
Not stated.

Bibliographic details

PubMedID
18599167

DOI
10.1016/j.vaccine.2008.05.048

Indexing Status
Subject indexing assigned by NLM

MeSH
Cost-Benefit Analysis; Humans; Models, Theoretical; Rabies /prevention & control; Rabies Vaccines /economics /immunology; United States

AccessionNumber
22008101732

Date bibliographic record published
31/03/2009

Date abstract record published
29/10/2013