An economic analysis of a pneumococcal vaccine programme in people aged over 64 years in a developed country setting

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Background Polysaccharide pneumococcal vaccination for older adults is being introduced in developed country settings. Evidence of protection by this vaccine against pneumococcal pneumonia, or confirmation that illness and death from bacteraemia are prevented, is currently limited. Decisions are often made based on partial information. We examined the policy implications by exploring the potential economic benefit to society and the health sector of pneumococcal vaccination in older adults.

Methods A model to estimate the potential cost savings and cost-effectiveness of a polysaccharide pneumococcal vaccine programme was based on costs collected from patients, the literature, and routine health-services data. The effect of a pneumococcal vaccine (compared with no vaccination) was examined in a hypothetical cohort aged over 64 years. The duration of protection was assumed to be 10 years, with or without a booster at 5 years.

Results If it were effective against morbidity from pneumococcal pneumonia, the main burden from pneumococcal disease, the vaccine could be cost-neutral to society or the health sector at low efficacy (28 and 37.5%, respectively, without boosting and with 70% coverage). If it were effective against morbidity from bacteraemia only, the vaccine’s efficacy would need to be 75 and 89%, respectively. If protection against both morbidity and mortality from pneumococcal bacteraemia was 50%, the net cost to society would be £2500 per year of life saved (£3365 from the health-sector perspective). Results were sensitive to incidence, case-fatality rates, and costs of illness.

Conclusions A vaccine with moderate efficacy against bacteraemic illness and death would be cost-effective. If it also protected against pneumonia, it would be cost-effective even if its efficacy were low.

Keywords Pneumococcal polysaccharide vaccine, pneumococcal vaccine—prevention and control, pneumococcal vaccine—economics, elderly, cost-effectiveness

In the UK the polysaccharide pneumococcal vaccine has been recommended for people with chronic respiratory, cardiovascular, renal, and liver disease, immunosuppression, and diabetes1 because of the 2–4-fold higher risk of pneumococcal disease and death.2 Incidence and mortality are higher in older than in younger adults, even when underlying medical conditions are absent.3 Influenza vaccination is recommended to all people aged over 64 years in an increasing number of settings. Pneumococcal vaccination is due to be phased in by 2005 in addition to the influenza vaccination programme for people over 64 years of age in England and Wales. In this article, we explore the economic efficiency of such a policy.

Economic evaluations that estimate net benefits to society from new interventions can help inform policy. Studies of polysaccharide pneumococcal vaccine efficacy suggest a 30–70% reduction in the risk of bacteraemia from pneumococcal infection, but data showing that actual illness or mortality from bacteraemia is prevented or that the vaccine protects against non-bacteraemic pneumonia are lacking.4,5 Research into the effectiveness of the
new 7-valent conjugate pneumococcal vaccine in older people is only just starting. Decisions have to be made based on partial evidence. In the absence of good evidence on efficacy, we used an approach that estimated the level of ‘efficacy’ of a vaccine against morbidity from pneumococcal infection that could be cost-saving. This value can be compared with efficacy studies as they become available. The cost-effectiveness of a new pneumococcal vaccine programme in people over 64 years old was also estimated using all the available evidence. The estimate assumed that the vaccine protected against both morbidity and mortality from (i) pneumococcal pneumonia and bacteraemic illness or (ii) pneumococcal bacteraemic illness only.

Research studies were conducted to estimate the costs of vaccine administration and the costs of treating pneumonia or of bacteraemia. Published or routine data sources on communicable disease surveillance, clinical trials, and hospital use were used for event rates, vaccine efficacy, the costs of the polysaccharide pneumococcal vaccine, and coverage.

Methods

Model

A cohort model was used in which the effect of an adult pneumococcal vaccination programme (compared with no programme) was estimated for a hypothetical cohort aged over 64 years of age, with the size, age, and sex structure of the population of England and Wales. The hypothetical cohort was followed up for 10 years, under scenarios (i) and (ii) above. The direct and indirect costs of the illnesses to patients and their carers in addition to the costs to the health sector were estimated to assess the economic impact of pneumococcal-related illness. These costs of illness were subtracted from the costs of the vaccine programme to estimate the cost per year of life potentially gained. As the costs of illness can be higher or lower than the values to society, we also refer to the values that society might place on the benefit of public health programmes in terms of societal willingness to pay for a year of life, an approach used by the US Food and Drug Administration (FDA).

Epidemiological parameters

Morbidity and mortality from pneumonia and bacteraemia

Details are given in Table 1. The incidence of pneumococcal pneumonia and mortality from non-bacteraemic pneumonia were derived from published studies. Laboratory reports in England and Wales (1996–99 inclusive), multiplied by 1.7 to adjust for underreporting, were used to estimate the incidence of pneumococcal bacteraemia. Mortality rates were based on a low case-fatality rate of 15% from a Californian study, as ascertainment of people who are less ill has increased over time in surveillance data. Cases in this study were possibly healthier than those in the general population but were actively ascertained from all microbiology specimens and had complete follow-up for mortality.

Life expectancy in those with pneumococcal disease

Because up to 80% of pneumococcal bacteraemia is reported in patients with underlying medical conditions, estimates of years of life gained were based on the mortality experience of people with such high-risk conditions. To estimate the expected life expectancy in people at high risk from pneumococcal disease, the UK General Practice Research Database (GPRD) from 1989 to 1999 was used to obtain age-specific and sex-specific mortality rates in a cohort of patients aged over 64 years at high risk compared with all people aged over 64 years. The GPRD study population had a similar proportion at high risk to the population-based sample in a national morbidity survey and a similar age and sex distribution to the general population. England and Wales life tables were adjusted by multiplying by the percentage reduction in life expectancy of people at high risk compared with all subjects in the GPRD study population.

Vaccine effectiveness, duration of effectiveness, and rates of adverse reactions

For the purposes of the cost-effectiveness analysis it was assumed that there was 50% efficacy against illness and death from pneumococcal bacteraemia based on reviews of trial data and observational studies. Meta-analyses of trials of the polysaccharide vaccine conducted in elderly people in developed country settings show no protective effect against pneumococcal pneumonia. This may be because of the poor specificity of a diagnosis of pneumonia, which reduces the ability to detect a protective effect of the vaccine against pneumonia even if it really exists. A statistically non-significant protective effect against bacteraemia of 30–47% is seen. Most observational studies indicate a higher, statistically significant, protective effect against bacteraemia ranging from 47 to 81%. This evidence is examined in detail in a recent systematic review, together with estimates of the duration of protection and rates of adverse events (see Table 1 for values).

Vaccine coverage

It was assumed that all those aged over 64 years were offered pneumococcal vaccine in Year 1 when they were offered influenza vaccination. Likely coverage was taken from the experience of the UK influenza vaccination programme. It was assumed that, each year, a further 5% of those who had not been vaccinated before would agree to be vaccinated.

Costs data for the model

Costs to the health sector and direct and indirect costs of the illnesses to patients and their carers (net societal costs) were included. Costs to the health sector included costs of the programme (vaccine, delivery of vaccine, adverse reactions, and administrative costs) and cost savings to hospitals and primary care. Cost estimates reflected opportunity costs as closely as possible. Costs were adjusted to 1998/99 prices using the National Heath Service Pay and Prices Index.

Vaccine programme costs. Resources that would need to be committed by central government to finance the programme were derived from the annual Department of Health allocations of monies to the influenza immunization programme for 2000–02, assuming that pneumococcal vaccination would incur similar central costs.

Administrative costs. Influenza and pneumococcal vaccines are delivered primarily by general practitioners (GPs), who provide ambulatory care for a defined list of patients. We conducted case studies to collect information on direct variable, fixed, and overhead costs in nine research general practices in the UK Medical Research Council General Practice Research Framework (MRC GPRF) (see ‘Detailed methods of costings’ the supplementary data available at IJE online).
Costs of illness from non-bacteraemic pneumonia. These were obtained from patients aged over 64 years with community-acquired pneumonia identified through the nine MRC GPRF research practices, which had fully computerized notes to ensure full ascertainment. Costs of illness with bacteraemic pneumococcal disease. Data were obtained on mean length of hospital stay and use of intensive care from routine Hospital Episode Statistics (HES) data for 1995–2000 for any pneumococcal disease-related diagnoses that occurred in any diagnostic field. Additional information was collected from cases who were part of a case–control study of invasive pneumococcal disease in southwestern England in 1999–2001. Cases, defined as an acute illness with isolation of Streptococcus pneumoniae from a normally sterile site, were identified through the enhanced surveillance system for bacteraemia. Production losses to society were calculated. Costs were discounted at 6% and health outcomes at 1.5%, consistent with UK Department of Health recommendations.

Sensitivity analyses

Sensitivity analyses were performed on parameters that were uncertain either because there was difficulty in identifying the costs or because the evidence for them was based on small numbers. Univariate and bivariate sensitivity analyses of the effect of changing some assumptions over plausible ranges were conducted.
Results

Vaccine programme costs
(Individual cost components are given in ‘Detailed results of costings’ in the supplementary data.) Administration costs are based on the average cost per vaccine delivered in practices using two nurses at a special standardized influenza vaccination session operating on weekdays or on a Saturday. Staff time spent on checking records for prior pneumococcal vaccination and administering the current polysaccharide pneumococcal vaccine varied between practices, with as little as half the overall time being spent administering influenza vaccination. In sensitivity analyses the resources used for polysaccharide pneumococcal vaccine delivery were therefore taken to range from being equal to the opportunity costs for administering influenza vaccination (£1.91) to half of this figure £0.96. The costs of adverse reactions were for those from the polysaccharide pneumococcal vaccine. The most efficient way to vaccinate was along with influenza vaccination. No additional costs to patients were included.

Cost savings
Cost savings were assumed from the costs of preventing pneumonia and bacteraemic disease. The incidence of community-acquired pneumonia in our study was 3.23 per 1000 people aged 65 or older, similar to other published rates33 (see ‘Detailed results of costings’ in the supplementary data). Response rates, parameters, and cost vectors used to estimate the costs of illness from pneumococcal bacteraemia are also given in ‘Detailed results of costings’ in the supplementary data.

Economic analysis of break-even costs
(See Table 2 and Figures 1 and 2.) From the net societal perspective a pneumococcal vaccine that protects against illness from both pneumonia and bacteraemia was cost-neutral if vaccine efficacy was a little over 28% and lasted 10 years with no need for a booster. This is based on the costs of the polysaccharide vaccine. A slightly higher vaccine efficacy of 37.5% would be needed for it to be cost-neutral if a booster were required at 5 years. From the health-sector perspective the equivalent required vaccine efficacy rates were 37.5 and 46% without or with a booster at 5 years, respectively.

If the vaccine was only protective against illness from bacteraemia, a 75% vaccine efficacy over 10 years would be cost-neutral to society; 89% from the health-sector perspective (Figure 2).

Cost-effectiveness analysis
An example of the cost-effectiveness of a vaccine that also prevented mortality was examined using an assumption of an efficacy of 37.5% against pneumonia and bacteraemia over 10 years with or without a booster at 5 years (Table 2). Costs savings were seen at the societal level. From the health-sector perspective the discounted cost per year of life would be £1360 with a booster at 5 years. With a vaccine efficacy of 37.5% against bacteraemia only and with a booster at 5 years, the costs to the health sector would be £8780 per discounted year of life saved.

Sensitivity analyses
With a vaccine that protected against illness from pneumonia and bacteraemia, the results were sensitive to varying the incidence of pneumonia (Table 3). If the incidence was 30% lower, a higher efficacy of 45.5 instead of 37.5% would be cost-neutral to the health sector. The indirect costs from pneumonia had a small effect on the vaccine efficacy required to maintain cost-neutrality from the societal viewpoint. A halving of the costs to patients and carers because of less time in bed or needing care suggested that vaccine efficacy, with a duration of protection of 10 years, needed to increase only slightly, to 31 from 28% efficacy.

If the vaccine protected only against illness from bacteraemia (Table 4), the conclusions based on cost-neutrality were sensitive to the costs of the illness. If the costs of illness from bacteraemia were 30% higher than the base case, a vaccine efficacy lasting 10 years against bacteraemic disease of 57 rather than 75% would be cost-neutral to society.

With a 37.5% rate of protection against death as well as illness from pneumonia and bacteraemia, the costs per year of life gained were sensitive to the incidence of disease and case-fatality rates. A cost of £4116 per discounted year of life saved was estimated if the vaccine was boosted at 5 years, based on the lower bounds of incidence of pneumonia and case-fatality rates.

Assuming a 50% rate of protection against death as well as illness from pneumococcal bacteraemia only, the costs per year of life gained were £2503 from the net societal perspective, if the protection lasted 10 years, and £5507 from the health sector perspective if a booster at 5 years was needed. The incidence of bacteraemia was inflated by 70%, which is a plausible estimate of the extent of underreporting. If the incidence was not inflated, the net costs to society of a vaccine with efficacy of 50% against bacteraemia for 10 years without a booster at 5 years rose from £2503 to £7877 per year of life gained.

Discussion
We conducted an economic analysis of a pneumococcal vaccine for use in elderly people using the available data (although there are important gaps in these data). An effect of the vaccine on clinical illness or mortality in more developed countries has yet to be clearly documented. In the unvaccinated, bacteraemia predicts a worse outcome from pneumococcal disease. Its predictive value in the vaccinated is not known, however. In the absence of good data on the efficacy of the polysaccharide vaccine, we constructed a model first to estimate the rate of ‘efficacy’ against illness that would be cost-saving. Evaluations of protection against illness by vaccination require smaller sample sizes and hence are easier to conduct than studies with death outcomes. Based on the costs of the current polysaccharide pneumococcal vaccine, a pneumococcal vaccine with coverage of 70% and vaccine effectiveness of just over 28% against illness from pneumonia and bacteraemia would incur zero costs to society. Slightly higher levels of effectiveness of a pneumococcal vaccine would generate savings for the health sector.

If it were also protective against mortality, our analysis suggests that an efficacy of 50% against illness and death from bacteraemia, with no effect on pneumonia, would cost £2500 per year of life from the societal perspective, £3365 from the
health-sector perspective without a booster, and £4646 and £5507 per year, respectively, with a booster at 5 years.

The findings here depend on the data and assumptions used to populate the model and its structure. In this article the likely efficacy of the vaccine as well as rates of illness that may arise are similar to those reported in previous work. This model can be adapted as new information (e.g. on the efficacy of a new or the existing vaccine, and on costs of a new vaccine) becomes available.

The main burden of disease from *S. pneumoniae* experienced by people aged over 64 years is pneumonia. The risk of pneumonia is not precisely known, but it is several-fold higher than for invasive pneumococcal disease or bacteraemia. The incidence of radiological pneumonia with culture-positive *S. pneumoniae* isolated from sterile sites or sputum was 3.8 per 1000 person-years in over-54-year-olds in the United States Veterans’ Administration’s trial, whereas the incidence of pneumococcal bacteraemia ranges from 0.6 per 1000 to 0.8 per 1000 in over-64-year-olds.

In the sensitivity analyses however, a 30% lower incidence of pneumonia made the vaccine efficacy needed for cost-neutrality only slightly higher. From the health-service perspective vaccine efficacy needed to rise a little, from 37.5% to 45.5%.

This project identified costs of illness to patients and carers from pneumococcal disease in adults. Although these costs do
not reflect the full societal benefit from the vaccine, they form an important socioeconomic burden on patients and carers. The indirect costs of illness to patients and carers for pneumonia were 29% (19% in those hospitalized, 79% in those not hospitalized) and for bacteraemic disease, 17% of the total costs of the illnesses. The indirect costs for bacteraemic pneumococcal disease appeared to be slightly more important than the costs of intensive care (both about one-sixth of the total cost per case of bacteraemia), though our sample sizes were rather small.

The costs of an illness may not be a good measure of the value society places on an intervention to prevent it. An approach used by the US FDA is to derive estimates of societal willingness to pay for a year of life saved. If the vaccine does prevent mortality and morbidity, this other calculus, that of willingness to pay for an extra year of life, gives even more favourable conclusions about the desirability of an effective pneumococcal vaccine. The costs of a pneumococcal vaccine programme in those aged over 64 years were well within values of a year of life saved used by UK agencies such as the Health and Safety Executive that estimate the willingness to pay to avoid a statistical death as £821656 per life saved at 1998/99 price levels.

Alternative data on hospital use were obtained from the HES, which record all discharges and deaths from National Health Service hospitals in England. They were a secondary source because the validity of cause-specific information in the HES has not been tested. The reliability of the coding is also only moderate.

**Figure 1** The net discounted cost per person vaccinated as a function of vaccine efficacy against bacteraemia and pneumonia

![Cost per person vaccinated from societal perspective](image)

![Cost per person vaccinated from health sector perspective](image)
The socioeconomic burden, as measured by indirect costs to patients and carers, is likely to be an underestimate as carers who were retired or unemployed may not have considered that there was an opportunity cost for their time. Our estimates of the number of days lost from illness, from primary studies of patients with pneumonia or bacteraemia, may also have been subject to recall bias because patients were surveyed a median of 49 days after their illness.

Previous economic analyses of the polysaccharide vaccine have examined benefits from the health-sector perspective only, assumed a certain efficacy against morbidity and mortality from bacteraemia, and in one case suggested that the current vaccine might prevent pneumonia and bronchopneumonia.

For comparability, we estimated the efficacy needed against only illness from bacteraemia to make pneumococcal vaccination cost-neutral to the health sector. It was 89% if

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**Figure 2** The net discounted cost per person vaccinated as a function of vaccine efficacy against bacteraemia only
Table 3  Sensitivity analyses of the cost-effectiveness of a pneumococcal vaccine effective against pneumococcal pneumonia and bacteraemia at 1998/99 prices (based on costs of the polysaccharide vaccine)

<table>
<thead>
<tr>
<th>Duration</th>
<th>10 years</th>
<th>10 years with booster dose at 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline: 37.5% vaccine efficacy against pneumonia and bacteraemia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained (£)</td>
<td>14</td>
<td>1360</td>
</tr>
<tr>
<td>Net cost to society per yr of life gained (£)</td>
<td>−1,503</td>
<td>−156</td>
</tr>
<tr>
<td><strong>Baseline + incidence of pneumonia 30% lower</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccine efficacy needed to be cost-neutral to health sector (%)</td>
<td>45.5</td>
<td>58.3</td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained (£)</td>
<td>1007</td>
<td>2607</td>
</tr>
<tr>
<td>Net cost to society per yr of life gained (£)</td>
<td>−400</td>
<td>1200</td>
</tr>
<tr>
<td><strong>Baseline + incidence of pneumonia 30% lower and case-fatality rate of 0.5%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained (£)</td>
<td>1390</td>
<td>4116</td>
</tr>
<tr>
<td>Net cost to society per yr of life gained (£)</td>
<td>−631</td>
<td>1895</td>
</tr>
<tr>
<td><strong>Baseline + case-fatality rate of bacteraemia reduced from 15 to 10%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained (£)</td>
<td>2254</td>
<td>5836</td>
</tr>
<tr>
<td>Net cost to society per yr of life gained (£)</td>
<td>−895</td>
<td>2687</td>
</tr>
<tr>
<td><strong>Baseline + indirect costs of pneumonia reduced by 50%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccine efficacy needed for it to be cost-saving to society (%)</td>
<td>31.5</td>
<td>41</td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained (£)</td>
<td>14</td>
<td>1360</td>
</tr>
<tr>
<td>Net cost to society per yr of life gained (£)</td>
<td>−947</td>
<td>399</td>
</tr>
</tbody>
</table>

Table 4  Sensitivity analyses of the cost-effectiveness of a pneumococcal vaccine effective against pneumococcal bacteraemia only at 1998/99 prices (based on costs of the polysaccharide vaccine)

<table>
<thead>
<tr>
<th>Duration</th>
<th>10 years</th>
<th>10 years with booster dose at 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Using upper bound of costs of illness from bacteraemia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccine efficacy that would make it cost-neutral to the health sector (%)</td>
<td>77</td>
<td>98</td>
</tr>
<tr>
<td>Vaccine efficacy that would make it cost-neutral to society (%)</td>
<td>57</td>
<td>73</td>
</tr>
<tr>
<td><strong>With a vaccine efficacy of 50% against bacteraemia only</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained</td>
<td>3 365</td>
<td>5 507</td>
</tr>
<tr>
<td>Cost to society per yr of life gained</td>
<td>2 503</td>
<td>4 646</td>
</tr>
<tr>
<td><strong>Vaccine efficacy 50% for bacteraemia only + incidence of bacteraemia not corrected by 1.7 for underreporting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained</td>
<td>8 738</td>
<td>12 381</td>
</tr>
<tr>
<td>Cost to society per yr of life gained</td>
<td>7 877</td>
<td>11 519</td>
</tr>
<tr>
<td><strong>Vaccine efficacy 50% for bacteraemia only + case-fatality rate reduced to 10% + incidence of bacteraemia not corrected by 1.7 for underreporting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained</td>
<td>13 107</td>
<td>18 371</td>
</tr>
<tr>
<td>Cost to society per yr of life gained</td>
<td>11 815</td>
<td>17 279</td>
</tr>
<tr>
<td><strong>Vaccine efficacy 50% for bacteraemia only + costs of bacteraemia at upper bound</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained</td>
<td>2 668</td>
<td>4 811</td>
</tr>
<tr>
<td>Cost to society per yr of life gained</td>
<td>945</td>
<td>3 088</td>
</tr>
<tr>
<td><strong>Vaccine efficacy 50% for bacteraemia only + costs of vaccine administration at lower bound</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained</td>
<td>2 842</td>
<td>4 737</td>
</tr>
<tr>
<td>Cost to society per yr of life gained</td>
<td>1 981</td>
<td>3 876</td>
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<tr>
<td><strong>Vaccine efficacy 50% for bacteraemia only + costs of bacteraemia at lower bound</strong></td>
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<td></td>
</tr>
<tr>
<td>Cost to health sector per yr of life gained</td>
<td>5 496</td>
<td>7 638</td>
</tr>
<tr>
<td>Cost to society per yr of life gained</td>
<td>5 065</td>
<td>7 208</td>
</tr>
</tbody>
</table>
This analysis suggests that a pneumococcal vaccine effective against pneumonia in all persons aged at least 65 years would be cost-neutral at quite low vaccine efficacy. If disease or death from pneumococcal bacteraemia alone are prevented, the cost-effectiveness of a pneumococcal vaccine would also be favourable based on the costs of the current polysaccharide vaccine. Another societal perspective, that of a willingness-to-pay estimate of the monetary value of a year of life saved, would mean that the benefit of the vaccine would be greater than the cost of implementation.

Further empirical work is required to assess the efficacy of any pneumococcal vaccine against ill-health and mortality as well as its impact on hospitalizations and the need for intensive care. This study, however, can be used to indicate the potential economic benefits as evidence of efficacy becomes available.

Acknowledgements

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KEY MESSAGES

- In England and Wales polysaccharide pneumococcal vaccination has been introduced, starting from August 2003 with those aged 80 years and over.
- Firm evidence of protection by the polysaccharide vaccine against pneumococcal pneumonia or confirmation that illness and death from bacteraemia are prevented is currently lacking.
- Decisions often have to be made based on partial information.
- This article explores the potential economic benefit of pneumococcal vaccination in older adults.
- If it were effective against the main burden from pneumococcal disease, pneumonia, the vaccine could be cost-neutral even at low efficacy.
- With confirmation of a suggested 50% protection against death and disease from pneumococcal bacteraemia, the net cost to society would be £2500 per year of life saved (£3365 from the health-sector perspective).

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