Cost-effectiveness of pneumococcal conjugate vaccination in the prevention of child mortality: an international economic analysis

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Summary
Background Routine vaccination of infants against Streptococcus pneumoniae (pneumococcus) needs substantial investment by governments and charitable organisations. Policymakers need information about the projected health benefits, costs, and cost-effectiveness of vaccination when considering these investments. Our aim was to incorporate these data into an economic analysis of pneumococcal vaccination of infants in countries eligible for financial support from the Global Alliance for Vaccines & Immunization (GAVI).

Methods We constructed a decision analysis model to compare pneumococcal vaccination of infants aged 6, 10, and 14 weeks with no vaccination in the 72 countries that were eligible as of 2005. We used published and unpublished data to estimate child mortality, effectiveness of pneumococcal conjugate vaccine, and vaccination rates.

Findings Pneumococcal vaccination at the rate of diphtheria–tetanus–pertussis vaccine coverage was projected to prevent 262,000 deaths per year (7%) in children aged 3–29 months in the 72 developing countries studied, thus averting 8·34 million disability-adjusted life years (DALYs) yearly. If every child could be reached, up to 407,000 deaths per year would be prevented. At a vaccine cost of International $5 per dose, vaccination would have a net cost of $383 million, a cost of $100 per DALY averted. Vaccination at this price was projected to be highly cost-effective in 68 of 72 countries when each country’s per head gross domestic product per DALY averted was used as a benchmark.

Interpretation At a vaccine cost of between $1 and $5 per dose, purchase and accelerated uptake of pneumococcal vaccine in the world’s poorest countries is projected to substantially reduce childhood mortality and to be highly cost-effective.

Introduction Vaccination of infants in the world’s poorest countries against Streptococcus pneumoniae (pneumococcus) has the potential to prevent many deaths, but would need substantial funding. Pneumonia and other respiratory infections cause about 2 million child deaths yearly, nearly all in developing countries.1 Most pneumonia deaths are believed to be due to bacterial pneumonia, and S pneumoniae is the most common cause of bacterial pneumonia in infants and young children.1 Additionally, pneumococcus often causes otitis media, bacteremia, sepsis, and meningitis in early childhood. Experience with other vaccines suggests that, without substantial global investment and coordinated effort, a conjugated pneumococcal vaccine is unlikely to reach children in developing countries during the next decade. Multilateral organisations, including the Global Alliance for Vaccines and Immunization (GAVI), have taken an increasingly important role in stimulating access to vaccines in poor countries.14

To decide whether and where to support introduction of pneumococcal vaccine, national and global policymakers need detailed information for justification of this investment. Previous studies of this topic,15 done before pneumococcal conjugate vaccine was available, do not have information from an important vaccine efficacy trial in The Gambia.15 Our aim was to incorporate these data into an economic analysis of pneumococcal vaccination of infants in GAVI-eligible countries (as of 2005) using a model applicable to many of the pneumococcal conjugated vaccine products in development. We did a decision analysis to generate global and country-specific information about the projected benefits, costs, and cost-effectiveness of pneumococcal vaccination in developing countries.

Methods Study design We constructed a decision analysis model using standard methods to assess lives saved, disability-adjusted life years (DALYs) averted, costs, and cost-effectiveness of pneumococcal conjugate vaccination of infants in the
world's poorest countries. These outcomes were assessed for each of the 72 countries that were eligible for GAVI support (panel)—countries with gross national income less than US $1000 per head and meeting other pre-specified criteria. A total of 76.9 million babies are born yearly in these GAVI-eligible countries. An expert panel with five members was convened and advised us on model structure and model inputs.

The decision tree (figure 1) included two strategies: vaccine purchase and provision, in which pneumococcal vaccine was purchased and provided to countries, via GAVI financial support, beginning in 2006; or no vaccine. No vaccine assumed that there would be no uptake of the vaccine, on the basis of previous experience in GAVI-eligible countries. In the GAVI financial support strategy, all children born were assigned a probability of death that depended on whether or not the child received the vaccine and on vaccine effectiveness against all-cause mortality. The death of a child resulted in the accrual of DALYs and death-related costs. Prevention of death by vaccination averted both DALYs and death-related costs. The vaccination programme resulted in costs related to purchase of vaccine and to programme administration.

We chose this model structure because data for childhood mortality and vaccination rates are available for all countries in this analysis. Data for intermediate outcomes, such as the incidence of pneumococcal infection or the distribution of pneumococcal serotypes, are available only from a few countries and are of variable quality. Hence, these outcomes were not incorporated into this model.

The set of assumptions used to do the primary analysis is termed the base-case analysis (table 1). Our base-case estimated vaccine effects on mortality alone; it was conservative in that it did not provide vaccination credit for reduction of non-fatal disease (eg, pneumonia needing hospital admission). The base-case analysis also did not assume any herd immunity effects—ie, protection of unvaccinated children or adults due to other individuals in the population being vaccinated.

We assumed that vaccine would be given according to the recommended schedule for diphtheria–tetanus– pertussis vaccines in GAVI-eligible countries (6, 10, and 14 weeks of age), and that vaccination rates in individual countries would be equal to the proportion of children reported to receive three doses of diphtheria–tetanus– pertussis vaccine in that country in 2003 (DTP3 rate). We also assumed that vaccination coverage would be 69% (range 37%–73%), vaccine effectiveness against all-cause mortality would be 7% (range 0%–16%), and vaccine efficacy against all-cause mortality would be 69% (range 32%–87%).

Table 1: Model assumptions for countries eligible for support from the Global Alliance for Vaccines and Immunization, by under-5 mortality rate per 1000 births

<table>
<thead>
<tr>
<th>Probability of dying between age 3 and 29 months</th>
<th>Vaccine effectiveness against all-cause mortality*</th>
<th>Vaccine efficacy against all-cause mortality†</th>
<th>Vaccination coverage rate</th>
<th>DALYs averted per death averted</th>
<th>Vaccine cost per dose†</th>
<th>Vaccine programme cost per dose†</th>
<th>Cost of treating fatal disease†</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;150</td>
<td>10.2%</td>
<td>7.4%</td>
<td>7.3%</td>
<td>30.8</td>
<td>5</td>
<td>0.34</td>
<td>150</td>
</tr>
<tr>
<td>100–149</td>
<td>5.6%</td>
<td>7.4%</td>
<td>13.1%</td>
<td>32.0</td>
<td>5</td>
<td>0.43</td>
<td>156</td>
</tr>
<tr>
<td>25–99</td>
<td>3.0%</td>
<td>3.7%</td>
<td>10.9%</td>
<td>33.1</td>
<td>5</td>
<td>0.45</td>
<td>231</td>
</tr>
<tr>
<td>&lt;25</td>
<td>0.4%</td>
<td>0.1%</td>
<td>3.2%</td>
<td>33.3</td>
<td>5</td>
<td>0.84</td>
<td>304</td>
</tr>
<tr>
<td>Range used in sensitivity analyses</td>
<td>75–125% base-case value</td>
<td>3–16%</td>
<td>Base-case value to 100%</td>
<td>Base-case value to 34.2</td>
<td>1–10</td>
<td>1–5 times</td>
<td>0.1 to 10 times base-case value</td>
</tr>
</tbody>
</table>

* = number of deaths prevented per 1000 children. † = % reduction in deaths. ‡ = International $.
Estimates of pneumococcal vaccine efficacy were available from several large, randomised controlled trials. Our analyses were based on the results of the trial done in The Gambia, because that study setting most closely resembled that of other GAVI-eligible countries. The Gambian trial is also unusual in that it provides an estimate of the efficacy of pneumococcal vaccination for prevention of all-cause child mortality.

In the trial, children were vaccinated through the existing Gambian expanded programme on immunisation at ages of 6, 10, and 14 weeks. Events were recorded between age 3 and 29 months. The vaccine’s efficacy for prevention of culture-confirmed invasive pneumococcal disease caused by vaccine serotypes was 77%, and vaccine serotypes accounted for 65% of invasive pneumococcal disease in the control group. Overall, a 50% reduction in culture-proven invasive pneumococcal disease was seen. 330 of 8189 children randomised to receive pneumococcal vaccine and 389 of the 8151 randomised to receive placebo died, which is an absolute reduction of 7.4 deaths prevented per 1000 vaccinated children during the period of observation.

We assumed that pneumococcal conjugate vaccine would be given in the same schedule as that used in the trial, and that vaccine would prevent deaths only between ages 3 and 29 months, the period observed in the trial. To extrapolate trial results to other countries, we assumed that vaccine efficacy against all-cause mortality would be greatest in those countries with high mortality rates in children aged under 5 years and lowest in countries with low mortality rates in this age group. This assumption was based on the finding that the proportion of childhood deaths caused by acute respiratory infection increases as mortality rate in children aged under 5 years increases, suggesting that the burden of pneumococcal disease, a common cause of acute respiratory infections could be highest in countries with highest child mortality.

In countries with mortality rates in children under the age of 5 years greater than that seen in the Gambian trial population (99 per 1000 livebirths), we assumed that vaccine efficacy against mortality would be capped at 7.4 deaths prevented per 1000 children. In countries with very high mortality rates in children aged under 5 years, this cap resulted in a low percentage reduction in deaths. Conversely, the projected vaccine efficacy against mortality was adjusted downwards from 7.4 per 1000 for any country with infant mortality rates less than or equal to 99 per 1000, on the basis of the ratio of the mortality rate in a specific country to that of the Gambian trial population. Unlike vaccine trials, in this analysis variations in vaccine efficacy mirror variations in the underlying risk of pneumococcal mortality in individual countries—not inherent variations in the biological activity of the vaccine. The probability of death between 3 and 29 months of age was derived from neonatal mortality data and standard life tables. We converted rates to probabilities using an exponential cumulative incidence function.

All costs are shown in International $ valued as for 2000, adjusted for purchasing power parity. The price at which vaccine will be available to GAVI or to developing countries is unknown. Our base-case used $5 per vaccine dose, under the assumption that the two-tiered pricing scheme used in international public vaccine markets will apply to pneumococcal vaccine. Vaccine programme costs were estimated under the assumption that pneumococcal vaccination would be incorporated into routine vaccine administration during infancy. Vaccine programme costs were derived from country-level financial sustainability plans data provided to GAVI by seven GAVI-eligible countries, and ranged between $0.27 and $0.97 per dose. These costs accounted for all non-vaccine costs (capital, transport, medical staff, injection supplies, training, and other expenses) for immunisations delivered via the expanded programme on immunisation.

The cost of a death preventable by pneumococcal vaccination was assumed to be equal to the cost of a case of pneumonia treated in hospital. Direct medical costs included days in hospital, medical staff time, diagnostic tests, and medications. Direct non-medical costs included transportation to health-care facilities and parent or caregiver time spent caring for a sick child. The costs of hospital days and medical staff time were derived from a set of WHO regional standard unit costs developed by choosing interventions that are cost effective (WHO-CHOICE) project. We assumed that 85% of hospital care was delivered in secondary facilities and 15% in tertiary facilities. WHO-CHOICE costs were applied to all countries on the basis of WHO region and were adjusted by ratios of public to private health care payment and urban to rural population.

The costs of diagnostic tests, medications, transportation, and parent time were derived from a detailed study of resource use in childhood pneumococcal disease done in India for the Children’s Vaccine Initiative (A Krishnan, personal communication). These costs were extrapolated to other countries, weighting costs by per head gross domestic product and ratios of public to private health care payment and urban to rural population.

Analyses

The base-case analysis estimated deaths averted by vaccination. Deaths averted were converted into years of life lost and DALYs, a standard measure used by WHO and World Bank in quantifying societal burden of disease. We used standard methods and assumptions, including age weighting in estimating DALYs. DALYs averted were based on estimates of life expectancy at age 1 year from standard life tables.

In secondary analysis, vaccine was also given credit for averting non-fatal pneumococcal meningitis, some of which could have resulted in permanent disability. Rates of meningitis-related permanent disability were taken...
from another Gambian study. Standard disability weights for sequelae (deafness, seizure disorder, motor deficit, and mental retardation) were applied.

The base-case analysis was done from a societal perspective, including all direct medical and non-medical costs borne by GAVI, governments, and families. Health outcomes and costs were discounted at 3% per year. We estimated cost-effectiveness ratios for all countries based on the formula: Cost-effectiveness ratio = (vaccine programme costs - cost of deaths averted)/DALYs averted.

The cost-effectiveness ratio numerator and denominator were calculated by multiplying probabilities in the decision tree by values for costs and DALYs, with standard decision analytical methods.

As a standard for comparison, we used WHO’s thresholds of cost-effective interventions. Interventions with cost-effectiveness ratios of less than three times the gross domestic product per head are cost-effective, and those with cost-effectiveness ratios below gross-domestic product per head are highly cost-effective.

To test the robustness of model results, we varied the assumptions over a plausible range in sensitivity analyses. We also varied assumptions using Monte Carlo probabilistic sensitivity analysis. In the probabilistic sensitivity analysis, each assumption was assigned a range of values it could have, and a frequency distribution over that range. Values for each assumption were randomly drawn from their distributions, and the model was run 10,000 times with these probability-sampled sets of assumptions. These methods and distributions are described in more detail in the webappendix.

We also did setting-specific secondary analyses, including a scenario in which vaccine was given credit for reducing hospital admissions and outpatient visits among vaccinated children with non-fatal pneumococcal disease and a scenario in which the risk of death and the probability of vaccination varied inversely by income strata. Details for these analytical methods are provided in the accompanying webappendix.

Analyses were done with DATAPro software, release 11 (TreeAge Inc, Williamstown, MA) and Microsoft Excel (Microsoft Corp, Redmond, WA).

Role of the funding source
GAVI provided data on vaccine programme costs for seven GAVI-eligible countries but had no role in study design, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data and had final responsibility for the decision to submit for publication.

Results
In the 72 GAVI-eligible countries, we projected that without pneumococcal vaccination, there would be 3.79 million deaths of children aged 3–29 months yearly. Pneumococcal vaccination was projected to prevent 262,000 of these deaths (7%) and avert 8.34 million DALYs annually if delivered at coverage rates similar to those for DTP3 (table 2). The greatest number of deaths could be averted in countries with both large birth cohorts and high childhood mortality. In India, Pakistan, Ethiopia, Tanzania, and Nigeria, 139,000 deaths could be averted, accounting for 53% of all deaths that could be averted in all GAVI-eligible countries.
If all 72 GAVI-eligible countries were to undertake pneumococcal vaccination at current DTP3 rates, 160.5 million doses of vaccine would be needed per year. Total programme costs would be about $882 million per year, including $802 million for vaccine purchase and $79.8 million for other vaccine programme costs, including administration, supplies, and additional medical staff time.

In our base-case analysis, which did not provide the vaccine programme credit for reduction of non-fatal disease, vaccination would avert direct medical and non-medical costs of $44.3 million in disease costs due to mortality. The net programme costs (vaccine programme costs minus disease costs) were $383 million. We used a human capital approach and gross national income per head as the value of a year’s lost productivity to estimate that $2.71 billion would be saved by averting 262,000 child deaths yearly. (This estimate was not used in cost-effectiveness calculations because the cost-effectiveness ratios already accounted for productivity losses as DALYs.) In a secondary analysis in which vaccination was assumed to reduce hospital admission rates, vaccination would avert $233 million annually in disease costs, resulting in net programme costs of $649 million per year.

Pneumococcal vaccination would cost $100 per DALY averted, on the basis of pooling costs and health outcomes for all 72 countries. The median country-level cost-effectiveness ratio was $75 per DALY averted (range, $56 in Azerbaijan to $14,800 in Cuba). At a vaccine price of $5 per dose, pneumococcal vaccination was projected to be cost-effective for 71 of the 72 (99%) countries, and highly cost-effective for 68 (94%) countries. At $2.50 per dose, pneumococcal vaccine was highly cost-effective in all countries apart from Cuba. Vaccination was not cost-saving over the vaccine cost range ($1 to $10 per dose) analysed.

Vaccination was very cost effective in countries with mortality rates in children aged under 5 years of more than 100 deaths per 1000 births. For example, cost-effectiveness ratios in Laos, Cambodia, and Haiti were $67 per DALY averted. Conversely, countries with mortality rates in children under 5 of less than or equal to 25 per 1000 births had the highest cost-effectiveness ratios. For example, cost-effectiveness ratios in Georgia, Sri Lanka, and Ukraine were $3433, $4211, and $5754 per DALY averted, respectively.

The projected cost-effectiveness of vaccination was most sensitive to estimates of vaccine efficacy against all-cause mortality and vaccine cost (figure 2). In countries with low childhood mortality, vaccine-dose cost was the main determinant of cost-effectiveness, but in countries with intermediate or high childhood mortality, both vaccine cost and efficacy had equal effect.

Results were moderately sensitive to the mortality rate, vaccine programme cost, and disease cost. Disease and vaccine programme costs were varied over wide ranges. When vaccine programme costs were increased five-fold from the country-specific base-case estimate, the cost-effectiveness ratio was $139 per DALY averted. When we reduced disease costs to a tenth of the country-specific base case estimate, the pooled cost-effectiveness ratio was $105 per DALY averted. Results were insensitive to vaccination rate.

The sensitivity of the analysis to vaccine efficacy was dependent on the price at which vaccine was offered (figure 3). At $1 per dose, the analysis was insensitive to vaccine efficacy. At this dose cost, conjugated pneumococcal vaccine remained a very cost-effective

![Figure 3: Effect of vaccine efficacy on the cost-effectiveness ratio, by vaccine cost](image)

Horizontal line=Mean gross domestic product per head.

![Figure 4: Effect of varying model assumptions on net costs and health outcomes in probabilistic sensitivity analysis](image)

DALYs=disability-adjusted life years.
intervention across all vaccine efficacies, with a cost-effectiveness ratio of $15–$101 per DALY. However, at $10 per dose, the analysis became fairly sensitive to vaccine efficacy, suggesting vaccine cost has a substantial influence on the overall analysis.

In the probabilistic sensitivity analysis, the number of DALYs averted by vaccination ranged from 3 million to 21 million DALYs and the net costs ranged from $491 million to $1320 million (figure 4). The cost-effectiveness ratio ranged from $31 to $286 per DALY averted, with a credible range (2.5–97.5 percentile) of $57–$185 per DALY averted. In all 10,000 simulations of the model, all estimates of costs and DALYs averted were greater than 0—ie, vaccination was neither cost-saving (net cost < 0) nor detrimental to health outcome (DALYs < 0). Quantitative estimates of sensitivity made with Spearman’s correlation coefficients identified vaccine efficacy against all-cause mortality and cost as the most important drivers of cost-effectiveness. The correlation coefficient for vaccine efficacy against all-cause mortality was -0.87 and was 0.37 for vaccine dose cost.

Access to vaccine and risk of mortality can vary by family income. Poorer children within a country could be at greater risk of dying and might be less likely to be vaccinated than rich children in the same country. Therefore, we did a secondary analysis, in which risk of death increased and vaccination rates decreased in lower income strata within each GAVI-eligible country. In this analysis, vaccine was least cost-effective in the higher income strata within a country, because of low mortality rates and high vaccine costs due to high vaccination rates. The converse was true in lower income strata within a country, with high mortality rates and low costs due to low vaccination rates. When pooled across all income strata, the effects of income stratification were slight, with a pooled cost-effectiveness ratio across all 72 GAVI-eligible countries of $101 per DALY averted.

In a separate analysis incorporating non-fatal disease, we assumed that vaccine prevented 7% of outpatient pneumonias, 35% of pneumonias that resulted in hospital admission, and 22% of pneumococcal meningitis that needed treatment in hospital. Under these assumptions, 1.16 million potential hospital admissions were averted. Cost-effectiveness ratios in countries with infant mortality rates of less than 25, 25–99, 100–149, and greater than or equal to 150 were $3532, $112, $56, and $60, respectively. The pooled cost-effectiveness ratio was $80 per DALY averted.

Discussion

At current vaccination rates, pneumococcal vaccination in GAVI-eligible countries could prevent 262,000 deaths yearly in children aged 3–29 months old, or about 7% of all potential deaths in this age group. Furthermore, at a price of $5 per dose, pneumococcal vaccine would be a highly cost-effective purchase in 68 of the 72 GAVI-eligible countries, on the basis of WHO standards for assessment of the economic value of health interventions. If vaccination coverage rates in these countries were 100%, 407,000 child deaths would be prevented every year.

Our analysis incorporated data from a clinical trial of conjugated pneumococcal vaccine. This trial benefited from a location and clinical setting that closely resemble typical conditions in many GAVI-eligible countries, compared with conditions at the sites of earlier trials, such as the USA, Finland, or urban South Africa. Our study focused on developing countries that are a policy priority, where GAVI has a commitment to promoting childhood immunisation and the introduction of selected new vaccines to childhood immunisation schedules.

Decisions about the introduction of conjugated pneumococcal vaccine in some of these countries will probably be made in the near future. Traditionally, new, expensive vaccines such as Haemophilus influenzae type b and hepatitis B have been slow to reach national immunisation programmes in poor countries, in part because of their cost. However, innovative financing mechanisms, such as advance purchase commitments, and international financing facilities, are under consideration for the purchase and provision of conjugated pneumococcal vaccine to accelerate their adoption by GAVI-eligible countries. This analysis lends weight to the assertion that such an investment would prove lifesaving and very cost effective in most of these countries.

Our results are in accord with earlier analyses of vaccines for developing countries that suggested that pneumococcal vaccination would have a cost-effectiveness ratio of $70 per quality-adjusted life-year or $58–$117 per life-year saved. The earlier studies had drawbacks in that they were done before the availability of new conjugate vaccines and did not have effectiveness data for either mortality or hospital admissions from studies like the Gambian trial. Our study concurs with the evidence that purchase and provision of pneumococcal conjugate vaccine for infants in the developing world is likely to be a highly cost-effective health investment.

This study’s primary result—that pneumococcal conjugate vaccine will prevent deaths and will be highly cost effective at $5 a dose—was robust when assumptions were varied in sensitivity analyses. Cost-effectiveness was driven by vaccine cost and vaccine efficacy and was less sensitive to all other assumptions.

Our primary analysis was conservative in several ways. It did not give vaccination credit for prevention of non-fatal disease. However, the sensitivity analysis that assumed that pneumococcal vaccination would prevent some hospital admissions suggested that this effect could potentially avert large numbers of such admissions and their costs. This finding is especially relevant for countries with well developed health care infrastructures and reduced child mortality rates. In these countries, the potential to avert morbidity could prove important.
in the making the decision whether or not to introduce vaccine. This analysis did not give vaccination credit for herd immunity protection. In the USA, routine pneumococcal vaccination of infants has led to large decreases in invasive pneumococcal disease in unvaccinated children and adults.10-12 However, whether developing countries, in which patterns of interaction and exposure differ, would show herd immunity effects of a similar magnitude is unclear. We also did not account for potential increases in disease caused by serotypes not covered by the vaccine or changes in the most common serotypes to those not covered by the vaccine, which could potentially degrade vaccine efficacy over time.13 The price at which pneumococcal conjugate vaccine will be offered to developing countries is unknown. However, a two-tiered pricing system has long been applied to vaccine prices in international public markets.14 We assumed that the same tiered pricing structure that results in lower costs for the eight antigens used in The Gambia would apply to pneumococcal conjugate vaccine as well. The base-case value used, $5 per dose, is a much higher price than those paid by UNICEF for diphtheria–tetanus–pertussis–H influenzae vaccine ($2.80) or hepatitis B vaccine ($0.62).15 Forecasts produced for GAVI’s PneumOAdIP suggest production will be adequate to meet demand if this vaccine is added to immunisation schedules in GAVI-eligible countries. The broad scope of this analysis needed a streamlined approach. The model was based on simple assumptions for which the best data exist, including the probability of death and vaccine efficacy against death. Our primary analysis did not attempt to estimate the reductions in the incidence of specific pneumococcal diseases such as pneumonia or meningitis. Our model was not dependent on pneumococcal serotype distribution, which varies between countries. Because our model does not need data for serotype distribution or the incidence of intermediate outcomes (ie, data only for mortality) it can be applied to all candidate pneumococcal conjugate vaccines with similar efficacies against mortality in developing world settings. However, the effect of pneumococcal vaccination will be dependent in part on the overlap between pneumococcal serotypes included in the vaccine and the local serotype distribution of disease-causing pneumococcal strains. At national level, local or regional data for pneumococcal disease burden and serotype distribution, as well as HIV prevalence (which modulates vaccine efficacy)16 will be useful in further refining the expected cost-effectiveness of vaccination. Decisions about purchase and provision of pneumococcal vaccine will be dependent on many factors in addition to cost-effectiveness, which include affordability, sustainability, opportunity costs, and programme capacity. However, the public health rationale for introduction of pneumococcal vaccination in poor countries is clearly based on the benefits recorded in recent trials. As this study makes evident, the economic argument for purchase of this vaccine in the developing world is equally compelling. Conflict of interest statement We declare that we have no conflict of interest. Acknowledgments We thank Robert Black, Logan Brenchel, Shams El Arifeen, Anne Schuchat, and Eric Simoes for their participation as expert panelists; and Thomas Cherian, James Daniel, Ulla Griffiths, William Haasdorff, Grace Lee, Marc Lipsitch, Katherine O’Brien, C Thomas Ray, Joshua Salomon, Radboud Damrje Tebbens, and Cynthia Whitney for thoughtful input. This work was done under collaborative arrangements between University of Medicine & Dentistry of New Jersey—New Jersey Medical School, Harvard Medical School, and the PneumOAdIP at Johns Hopkins Bloomberg School of Public Health. It was funded in full by the Global Alliance for Vaccines and Immunization and The Vaccine Fund. It was presented in part at the Fourth International Symposium of Pneumococci and Pneumococcal Diseases (Helsinki, Finland, May 10, 2004) and the 42nd Annual Meeting of the Infectious Diseases Society of America (Boston, USA, Oct 2, 2004). Contributors A Sinha, O Levine, M D Knoll, and T A Lieu designed the study. Data collection was done by A Sinha, M D Knoll, F Muhih, and T A Lieu. Data were analysed by A Sinha, F Muhih, M D Knoll, and T A Lieu and were interpreted by A Sinha, O Levine, M D Knoll, and T A Lieu. The manuscript was written by A Sinha, M D Knoll, and T A Lieu and was edited by O Levine. All authors were involved in the decision to submit the manuscript for publication. For PneumOAdIP see http://www.pneumoAdIP.org References 1 Williams BG, Gouve e D, Boschi-Pinto C, Bryce J, Dye C. Estimates of world-wide distribution of child deaths from acute respiratory infections. Lancet Infect Dis 2002; 2: 25–32. 2 Shann P. Etiology of severe pneumonia in children in developing countries. Pediatr Infect Dis J 1986; 5: 247–52. 3 Technical bases for the WHO recommendations on the management of pneumonia in children at first-level health facilities. Geneva: World Health Organization, 1992. 4 Levine OS, Cherian T, Shah R, Bateson A. PneumOAdIP: an example of translational research to accelerate pneumococcal vaccination in developing countries. J Health Popul Nutr 2004; 22: 268–74. 5 Hinman AR. Immunization, equity, and human rights. Am J Prev Med 2004; 26: 84–88. 6 Lieu TA, McGuire TG, Hinman AR. Overcoming economic barriers to the optimal use of vaccines. 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