HNP DISCUSSION PAPER

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## Health, Nutrition and Population (HNP) Discussion Paper

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# Health, Nutrition and Population (HNP) Discussion Paper

## Cost-effectiveness and Financial Consequences of New Vaccine Introduction in Pakistan

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This study was conducted with the support of the GAVI Alliance Trust Fund to the World Bank.

**Abstract**: Pakistan has one of the highest infant mortality rates in the world, and over 50 percent of deaths in post-neonatal children are attributable to pneumonia, diarrhea, or meningitis—diseases that can be prevented through vaccination. The purpose of the study is to compare the cost-effectiveness and financial implications of introducing pneumococcal (PCV-10), rotavirus (Rota-Teq), and Haemophilus influenza type B (Hib) vaccines in Pakistan.

The cost-effectiveness analysis was conducted using the Tri-Vac model, which is a static model that estimates the burden of disease and the costs of treatment and for the immunization program of children up to five years old in ten annual birth cohorts (2010 to 2019). Sensitivity analyses were conducted testing key assumptions related to disease burden, vaccine efficacy, and vaccine cost. The analysis of financial implications included a projection of cold chain needs and costs associated with the introduction of each new vaccine, as well as the financial outlays required by the government. Sensitivity testing was also conducted on major assumptions.

All three vaccines were found to be cost-effective, with Hib vaccine the most cost-effective option at $22 per disability-adjusted-life-year (DALY). The cost-effectiveness figures for PCV and rotavirus vaccines were $225/DALY and $201/DALY, respectively. Sensitivity testing did not significantly alter the results.

The combined financial requirement for the three new vaccines would peak in 2017 if GAVI assistance reduced to five rather than eight years ($213m). This cost would account for 40 percent of national immunization expenditures, and 15 percent of government health expenditures. Required cold chain investments would be small relative to the expenditure on vaccines, and represents a good return on investment.

While the investment would be worthwhile from an economic perspective, introducing all three vaccines in Pakistan will present financial challenges unless overall health spending increases. Careful consideration needs to be given to long-term financing after GAVI support ends.

**Keywords**: cost-effectiveness, vaccine, sustainability, Pakistan

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## Abbreviations

| | |
|---|---|
| AHP | Accelerated Health Program of Pakistan |
| CI | Confidence Interval |
| cMYP | Comprehensive Multi-Year Plan |
| DALY | Disability-Adjusted-Life-Years |
| DTP3 | Diphtheria-Tetanus-Pertussis vaccine, 3rd dose |
| EPI | Expanded Program on Immunization |
| GDP | Gross Domestic Product |
| GHE | Government Health Expenditure |
| GOP | Government of Pakistan |
| HDNHE | Human Development Network, Health, Nutrition, and Population |
| Hib | Haeomophilus influenza type b vaccine |
| ICER | Incremental Cost-effectiveness Ratio |
| LSHTM | London School of Hygiene and Tropical Medicine |
| NHA | National Health Accounts |
| NIP | National Immunization Program |
| NPNM | Non-Pneumonia, Non-Meningitis |
| PAHO | Pan American Health Organization |
| PCV | Pneumococcal Conjugate Vaccine |
| PDHS | Pakistan Demographic and Health Survey |
| RV | Rotavirus Vaccine |
| UNICEF | United Nations Children's Fund |
| WHO | World Health Organization |

# PART I: INTRODUCTION

## 1.1 Cost and Financing of Immunization Programs

Historically, vaccines have been among the "best buys" in public health (SOWVI 2009). Immunization with traditional EPI antigens has been one of the most cost-effective interventions, accounting for $2 to $20 per year of healthy life gained (Brenzel et al., 2006).[1] Ranges in cost-effectiveness estimates are related to differences in disease burden, coverage or scale of a program; unit prices of key inputs such as vaccines; and, the type of delivery system used to provide services (Lydon et al., 2008; Brenzel and Claquin, 1994; Kaddar et al., 2004). Although more expensive per unit, the new vaccines, such as pneumococcal, rotavirus, and Haemophilus influenza type b vaccines, have been found to be cost-effective in a variety of contexts (Fischer et al., 2005; Sinha et al., 2007; Reingans et al., 2009; Wang XY et al., 2009).

New vaccine introduction has implications for the costs and long-run affordability of national immunization programs. New vaccines are the single largest cost driver, accounting for at least 50 percent of total immunization expenditure. Resources required for routine immunization in the poorest countries are expected to nearly triple from an average of $6 to $18 per infant by 2010, perhaps rising to as much as $30 per infant by 2015 (Lydon et al., 2008). This represents an average increase in the share of government health expenditure for immunization, from 2.4 to 3.7 percent.[2] Given the multiple demands for healthcare and limited resources in low-income countries, this share may not be affordable or sustainable (SOWVI, 2009). In recent years, nearly twenty of the poorest countries have seen a drop in immunization financing by governments that suggest possible substitution in favor of donor financing and greater donor dependency for national programs (Lydon et al., 2008).

Pakistan's large population, high fertility, budget constraints and service delivery challenges, make the cost-effectiveness and affordability of new vaccines virtually unaffordable. Factors such as the prevalence and severity of diseases, effectiveness and cost of vaccines, and potential health care costs avoided through vaccination need to be considered.

## 1.2 The Expanded Program on Immunization (EPI) in Pakistan

The Expanded Program on Immunization (EPI) started in Pakistan in December 1976 following the Smallpox Eradication Program. Initially, the program began as a pilot project in major urban areas. In 1979, the first national five-year program was launched to provide universal vaccination coverage for all children under five years old. Services were to be provided by static health centers at district, tehsil, and lower levels, staffed by vaccinators hired by local district units for the Smallpox Eradication Program.

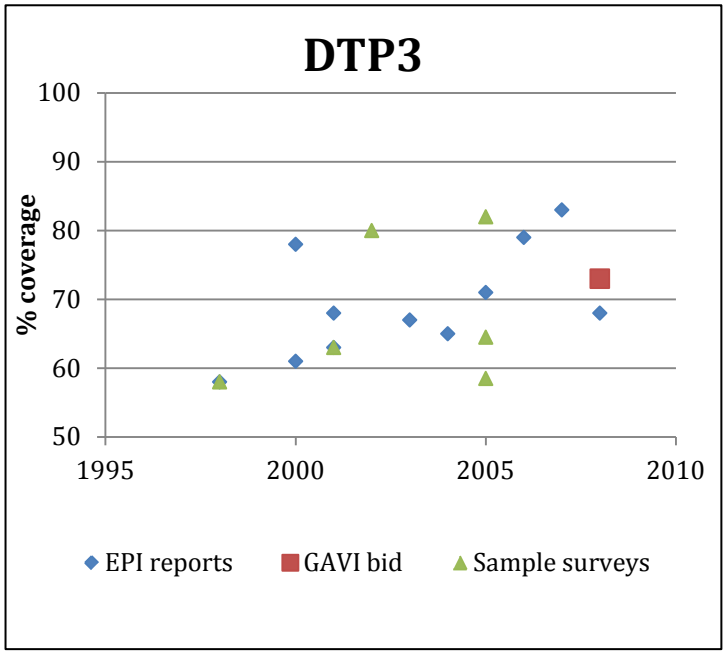
[1] Traditional immunizations include measles, diphtheria, tetanus, pertussis, oral polio and BCG.

[2] This average increase masks the situation in eight countries, where the figure exceeds 10.0 percent, and in two countries where immunization accounts for nearly one-fifth of government health expenditures.

By 1982, immunization coverage was still very low (5 percent) and the program required further strengthening. The following year, the Accelerated Health Program (AHP) was launched, with the EPI as one of the components.[3] Under the AHP, the EPI provided immunization against six vaccine-preventable diseases (diphtheria, tetanus, pertussis, polio, measles, and tuberculosis). Services were delivered by field workers under the control of the Provincial Health Department, resulting in improved implementation of the program.

Currently, policy, strategic guidance, procurement, supply and finance of vaccines and disposable syringes are provided by the federal government, while the implementation of the program (including staff salaries) and provision of other supplies are covered by the provinces. All program staff are paid from the recurrent budget for health.[4]

**Figure 1. Historical and Projected DTP3 Coverage in Pakistan From Various Sources (Children 12-23 Months)**




*Source:* UNICEF 2008

Figure 1 shows estimates of coverage for the third dose of diphtheria-tetanus-pertusis (DTP3) vaccine since 1995 from different sources, including estimates used as the basis for Pakistan's application to the GAVI Alliance for pentavalent vaccine support. [5] In 2005, DTP3 coverage

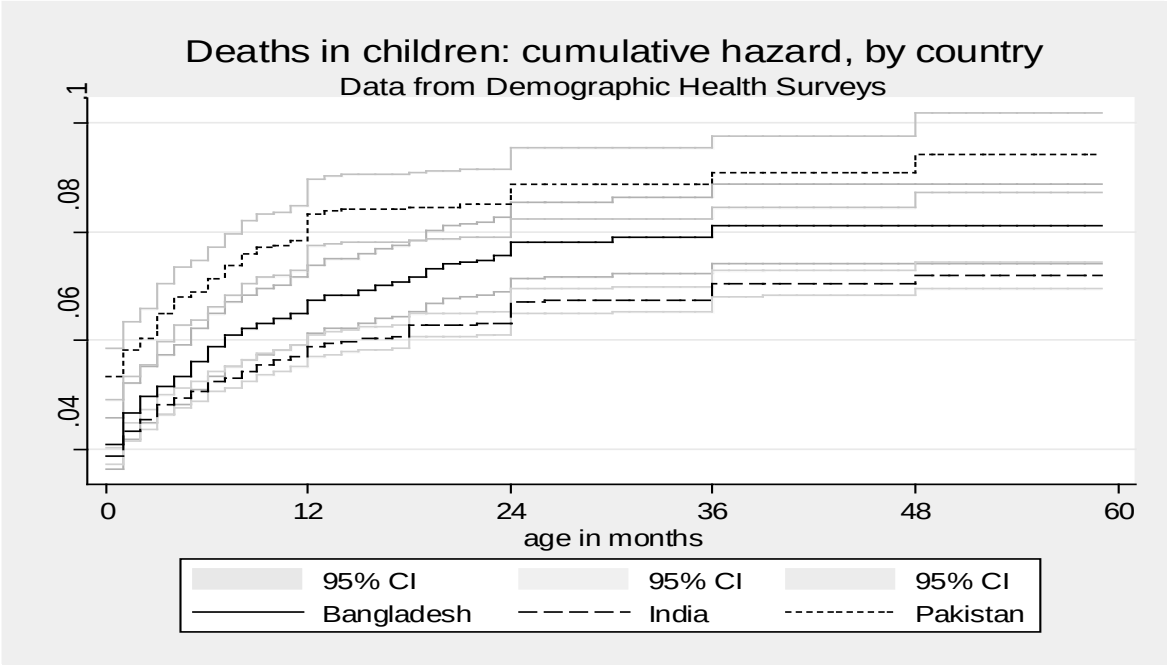
[3] The other health programs included control of diarrheal disease and training of traditional birth attendants.
[4] Recently a small number of vaccinators on the provincial government payroll have been supported by funds from the GAVI Alliance.
[5] The pentavalent vaccine includes DTP, Hepatitis B, and Haemophilus influenza type B antigens. Children receive all antigens in one injection.

ranged from less than 60 percent to over 80 percent depending upon the source of information and method of data collection. WHO-UNICEF best estimates of DTP3 coverage for Pakistan are 85 percent as of 2009, up from 73 percent in 2008 (WHO, Reported estimates of vaccine coverage, last accessed on March 22, 2011).

## 1.3 Childhood Mortality and Morbidity in Pakistan

Pakistan has the eighth highest newborn death rate in the world (UNICEF, 2009). In addition, approximately 10 percent of children born in Pakistan die before they reach their fifth birthday. Figure 2 shows that the infant mortality rate in Pakistan was 78 per 1,000 live births in 2007 (PHDS, 2006/07). Child mortality was 94 per 1000 in 2006. These figures are high in comparison to other countries in the region, such as Bangladesh and India.

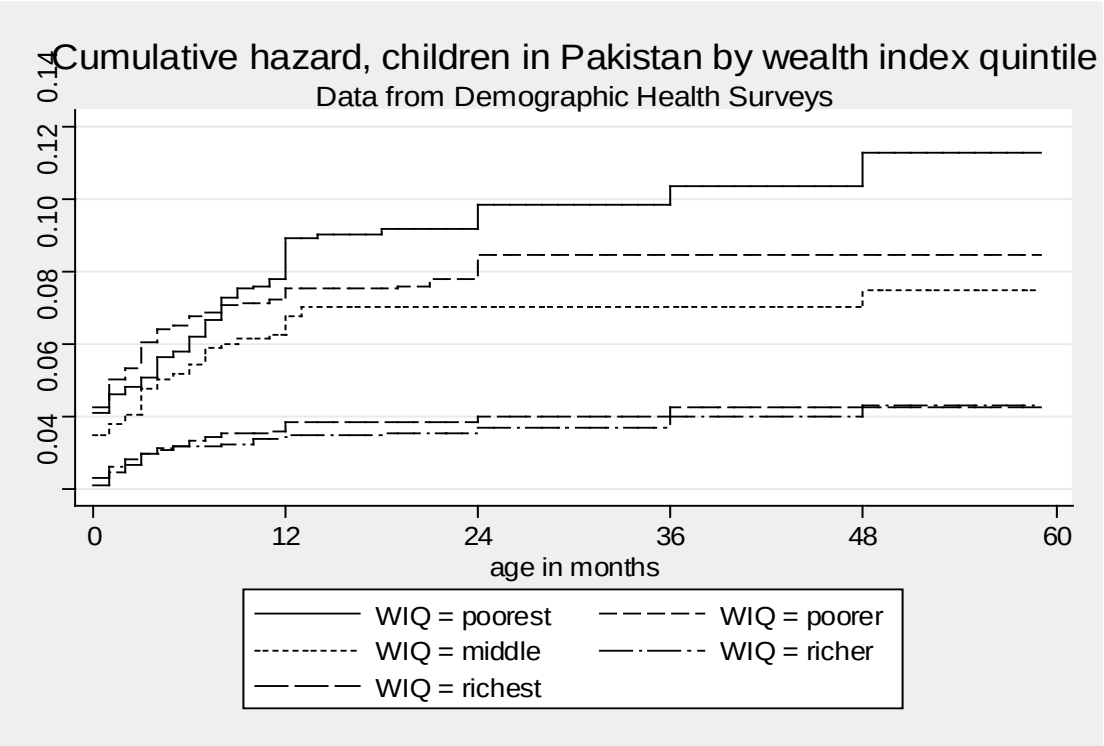
**Figure 2. Deaths in Children in Pakistan 2006/7 Compared to Other Countries in the Southeast Asian region**




*Source*: authors' analyses of PHDS data.

Data from the Pakistan Demographic Health Surveys (PDHS) and other sources suggest that death rates are particularly high among the poor in rural areas where access to medical care is limited (figure 3). By regional and international standards, the rate of decline in under-5 mortality is low.

**Figure 3. Child Mortality in Pakistan by Wealth Quintile**




*Source*: authors' analyses of PDHS data.

There is no comprehensive system of death registration in Pakistan. According to verbal autopsy reports, about half of all the deaths in post-neonatal children were caused by pneumonia, meningitis or diarrhea (Table 1). One estimate suggests that over 50 percent of deaths in post-neonatal children are attributable to pneumonia, diarrhea, or meningitis (PDHS, 2006/07).

**Table 1. Causes of Death for Children in Pakistan, 2005 (Percentages by Age)**

| Cause | Age of Child at Death | | | |
|---|---|---|---|---|
| | <1 month | 1-11 months | 1-4 years | All <5 years |
| Pneumonia | 6.3 | 25.7 | 16.9 | 13.3 |
| Meningitis | 0.8 | 9.1 | 6.6 | 4.0 |
| Diarrhea | 1.0 | 26.9 | 17.7 | 10.8 |
| Subtotal | 8.1 | 61.7 | 41.2 | 28.1 |
| Other/unknown cause | 91.9 | 38.3 | 58.5 | 71.9 |
| Total | 100 | 100 | 100 | 100 |
| Number of deaths | 1,651 | 788 | 503 | 2,043 |

*Source*: adapted from Bhutta ZA, Cross A, Farrukh R, and Zaheer Z. 2008.

In Pakistan, access to timely and effective treatment for these diseases is difficult for households, particularly in rural areas. However, a new generation of vaccines has become available. Two of these vaccines protect against Haemophillus influenza type b (Hib) and pneumococcal infections, both of which cause pneumonia and meningitis; and one vaccine protects against rotavirus, a cause of diarrhea. Vaccination can offer an effective way of reducing the burden of disease in those vaccinated, and can benefit others by reducing exposure to infection more generally.

"Positive externalities" of this kind provide the economic justification for government financial investment in vaccination programs.

The GAVI Alliance is a partnership between multilateral, bilateral, civil society, private sector, and academic agencies seeking to save children's lives and promote health by increasing access to immunization in poor countries (GAVI Alliance, 2011). It is aa funding mechanism available to low-income countries for the purchase of new and under-utilized vaccines. Since 2000, the GAVI Alliance has provided millions of doses of vaccines, resulting in major reductions in disease, such as measles, and prevention of an estimated five million child deaths.

## 1.4 Purpose of the study

Following the availability of new vaccines through the GAVI Alliance, the Government of Pakistan (GOP) requested an analysis of the cost-effectiveness and financial implications of introducing pneumococcal conjugate vaccine (PCV-10) and rotavirus (RV) vaccines to the birth cohort. This was done in comparison with the cost-effectiveness and financial requirements for Hib vaccine that had been introduced in Pakistan in 2009 through the GAVI Alliance. Using cohort-based modeling techniques, the study provides information to assist the GOP do the following:

- evaluate the tradeoffs of introducing new vaccines;
- prioritize the introduction of new vaccines in the EPI; and,
- develop credible estimates on costs and financing for the Ministry of Finance and the Planning Commission for budgeting and planning purposes.

The study was designed, managed and commissioned by the Human Development Network, Health, Nutrition, and Population Unit (HDNHE) of the World Bank. Researchers at the London School of Hygiene and Tropical Medicine (LSHTM) were contracted to conduct the comparative cost-effectiveness analysis. Independent consultants were recruited to undertake the financial evaluation and to assist with data collection and analysis of the health system in Pakistan. The study commenced in 2008, with fieldwork conducted in 2009.

# PART II: COMPARATIVE COST-EFFECTIVENESS ANALYSIS

This section describes the methods undertaken for evaluating the cost-effectiveness and financial implications of introducing the 10-valent pneumococcal vaccine (2-dose schedule), RotaTeq oral vaccine (3-dose schedule); and the Hib component of the pentavalent vaccine currently in use in Pakistan. The pentavalent vaccine provided the benchmark against which the PCV and RV results were compared.

## Section 2.1: Methods

### *2.1.1. Tri-Vac Model*

Since the GoP will be taking decisions about vaccine introduction, the analysis was performed from a government perspective. [6] The comparative cost-effectiveness analysis was performed using the Tri-Vac Model, which was developed at the London School of Hygiene and Tropical Medicine (LSHTM) for the ProVac Initiative of the Pan American Health Organization (PAHO) and the GAVI Hib Initiative (http://www.hibaction.org). The Trivac model was designed for direct decision support.[7] It provides a framework within which data and assumptions are explicit, and which allows policy makers to explore the implications of choosing different options under different scenarios in facilitated workshops. The idea is that policy makers are more likely to make good use of the evidence available if they understand what the model does. Annex 1 illustrates the structure of the Tri-Vac model.

A static compartment model, the Trivac model estimates the burden of disease; the costs of treatment; and the cost of the National Immunization Program (NIP) with and without each new vaccine for children up to five years old in ten successive annual birth cohorts (2010 to 2019). [8] One-dimensional and probabilistic sensitivity analyses were conducted on the original baseline scenario, testing key assumptions related to disease burden, vaccine efficacy, and vaccine cost. In the sensitivity analysis, the model incorporates mid, low, and high price trajectories for the pentavalent vaccine. The low trajectory involves a faster fall in pentavalent price after 2015, and the high-price trajectory maintains the same price from 2015 onwards. The duration of GAVI Alliance support varies from a baseline of five years to eight years.

The Tri-Vac Model allows for improvements in vaccine coverage over time. These are modelled by specifying a long-term target value for coverage (for example 90 percent), and increasing baseline coverage rates for DTP3 by a fixed percentage each year in order to reach the target coverage rate. In addition, the model incorporates declines in serotype coverage with time

[6] This excludes out-of pocket health care costs for parents or carers, and benefits accruing to people other than children less than five years of age.

[7] The model is based on Excel, and to that extent it is transportable, accessible and transparent. At the same time it includes facilities for interactive data input, scenario analysis and sensitivity analysis (including probabilistic) programmed using Visual Basic, which enhance its usability as a decision support tool.

[8] In this context a *static* model is one in which the rate of transmission of the infection is not determined within the model, i.e., the risk of infection does not change over time in response to modelled changes in the incidence or prevalence of infection. In *compartment* models, the movement between discrete 'health states' (e.g., well, infected, dead) is modelled for population groups, whereas in *micro-simulation* models this is done for individuals.

(serotype replacement) by a fixed percentage per year, and declines in vaccine efficacy with age (waning efficacy), by a fixed percentage per year. Through a multiplier, the model accounts for the indirect benefits of vaccination or the herd effect.

To determine the range of extreme values, parameters were bundled into favorable and unfavorable combined scenarios. The favorable scenario incorporated a high burden of disease, vaccine efficacy, serotype coverage, and health care costs avoided, with the unfavorable scenario being low in all these respects. [9]

### *2.1.2 Incremental cost-effectiveness ratios*

Incremental cost-effectiveness ratios (ICERs) were estimated for each vaccine over the 10-year period. The incremental disease burden and costs are estimated by the difference with and without the new vaccine:

| | | |
|---|---|---|
| **ICER** | **=** | **Net vaccine cost / Net benefits** |
| **Net vaccine cost** | **=** | **Total program cost - total health care costs avoided** |

The net cost per vaccine is the marginal cost of adding the new vaccine to the NIP minus the total health care costs avoided based on estimates from the WHO-Choice model [10] and the health economics literature (WHO, 2008). Estimates for health care costs avoided are notional to the extent that they could be available to government to reallocate to other uses in the health care system.

The total cost of the NIP was based on the vaccine price per dose and number of doses required per child, plus delivery, administration, and wastage costs. If applicable, costs were also included for safety boxes and syringes. It was assumed that new vaccines were delivered at the same time as other vaccines in the EPI, and only staff and transport costs additional to those for administering DTP-HepB were included. Capital items, such as cold chain infrastructure costs, were handled in the financial analysis only.

Benefits of the vaccines included reductions in the burden of disease as measured by numbers of deaths, episodes and sequelae of disease, and Disability-Adjusted-Life-Years (DALYs). The diseases of interest for the analysis were pneumonia, meningitis, other bacterial infections labelled collectively as “non-pneumonia non-meningitis” (NPNM), otitis media, and diarrhea.

[9] According to the Global Serotype Project survey, PCV10 should cover about 70 percent of the distribution of serotypes in Asian studies (Johnson HL, et al, 2010). The study assumed the same level of vaccine efficiency for PCV10 as for PCV7, in the range of 52 percent to 70 percent, with no cross-protection. More recent studies in Africa and Asia show a low efficacy in the range 40-50 percent, and these figures were used in sensitivity testing, assuming full cross-protection.

[10] http://www.who.int/healthinfo/global_burden_disease/tools_national/en/index.html.

### *2.1.3 Parameter estimation and verification*

Prior to populating the Tri-Vac model with parameter estimates, a survey of the literature was conducted and point and interval estimates for each parameter was presented to a team of Pakistani experts for corroboration and verification (Sanderson et al., 2010). A Delphi process was conducted, which refined the parameter estimates for use in the model. For the baseline scenarios for Hib and PCV, epidemiological estimates from the WHO Global Burden of Disease program were used (Watt et al., 2009; O'Brien et al., 2009). Because WHO-commissioned estimates on the numbers of deaths from rotavirus diarrhea were published, but not for the non-fatal burden, parameter values consistent with the WHO mortality estimates, the regional literature and comments from key informants, were produced (Parashar et al., 2009).

Vaccine price estimates for the period 2010-15 were based on weighted average supply prices that include both freight and shipping costs. [11] Price estimates also were expected to decline over the study period, and assumptions were made in the model about price trajectories based on information provided by the GAVI Alliance.

The unit prices used in the analysis are given in table 2. The unit price of Hib vaccine in 2010 was estimated as the difference between the cost of the pentavalent vaccine currently in use in Pakistan (US$3.20 per dose), and the unit price of the quadravalent DTP-HepB vaccine (US$0.65 per dose). The model assumes that the 2010 price of the pentavalent vaccine would decline by 10 percent per year reaching US$1.85 per dose in 2015. In addition to paying the full price of the new vaccine, the analysis also incorporated the financing requirements for the GOP under the Co-financing Policy of the GAVI Alliance for the duration of GAVI support. Parameters used in different scenarios in the comparative cost-effectiveness analysis are found in annex 2.

**Table 2. Vaccine Price Assumptions for Different Model Scenarios (US$ per dose)**

| | Hib | | | | | PCV | | | | | RV | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Mid* | *High* | *Low* | *Co-fin 8* | *Co-fin 5* | *Mid* | *High* | *Low* | *Co-fin 8* | *Co-fin 5* | *Mid* | *High* | *Low* | *Co-fin 8* | *Co-fin 5* |
| 2010 | $3.20 | | | $0.30 | $0.30 | $7.19 | | | $0.20 | $0.20 | $5.27 | | | $0.20 | $0.20 |
| 2011 | $2.91 | | | $0.30 | $0.30 | $7.19 | | | $0.20 | $0.20 | $5.27 | | | $0.20 | $0.20 |
| 2012 | $2.62 | | | $0.30 | $0.30 | $7.19 | | | $0.20 | $0.20 | $5.27 | | | $0.20 | $0.20 |
| 2013 | $2.32 | | | $0.30 | $0.30 | $6.59 | | | $0.20 | $0.20 | $4.33 | | | $0.20 | $0.20 |
| 2014 | $2.03 | | | $0.30 | $0.30 | $5.78 | | | $0.20 | $0.20 | $3.33 | | | $0.20 | $0.20 |
| 2015 | $1.85 | | | $0.30 | $1.85 | $5.80 | | | $0.20 | $5.80 | $2.67 | | | $0.20 | $2.67 |
| 2016 | $1.66 | $1.85 | $1.57 | $0.30 | $1.66 | $5.18 | $5.80 | $4.93 | $0.20 | $5.18 | $2.42 | $2.67 | $2.35 | $0.20 | $2.42 |
| 2017 | $1.49 | $1.85 | $1.34 | $0.30 | $1.49 | $5.11 | $5.80 | $4.19 | $0.20 | $5.11 | $2.19 | $2.67 | $1.99 | $0.20 | $2.19 |
| 2018 | $1.33 | $1.85 | $1.14 | $1.33 | $1.33 | $4.45 | $5.80 | $3.56 | $4.45 | $4.45 | $1.98 | $2.67 | $1.69 | $1.98 | $1.98 |
| 2019 | $1.19 | $1.85 | $0.97 | $1.19 | $1.19 | $4.22 | $5.80 | $3.03 | $4.22 | $4.22 | $1.79 | $2.67 | $1.44 | $1.79 | $1.79 |
| 2020 | $1.07 | $1.85 | $0.82 | $1.07 | $1.07 | $4.30 | $5.80 | $2.57 | $4.30 | $4.30 | $1.62 | $2.67 | $1.22 | $1.62 | $1.62 |

*Note*: Cofinancing 8 or 5 refers to the number of years Pakistan would be co-financing their new vaccines.

[11] Hib and rotavirus vaccine prices were obtained from UNICEF Supply Division, and price for PCV10 was provided by the GAVI Alliance.

### *2.1.4 Limitations of the methods for the cost-effectiveness analysis*

The analysis is based on a static, rather than a dynamic model. [12] This means that the incidence of infection in vaccinated children is reduced in line with vaccine efficacy, but in unvaccinated children, the incidence remains unchanged. This may not reflect reality because a decrease in incidence among vaccinated children reduces the risk among the unvaccinated. As a result, baseline estimates from this model will underestimate DALYs averted and overestimate the costs per DALY averted.

The potential impact of indirect effects was evaluated in the sensitivity analysis by adding a percentage to the direct effect, which means that the scale of the "boost" to direct effects is fixed, and the boost only applies to children in vaccinated cohorts. While these assumptions may have limitations, the approach is justifiable for the following reasons. First, if an intervention is cost-effective without indirect effects, including them could only make them more cost-effective. Second, most of the benefits of vaccination in low-income countries come from preventing fatal disease in children aged less than 24 months, and our model captures most of these. Third, if program coverage and vaccine effectiveness are high, the scope for indirect effects is small once the program has been established, as most of the disease will be prevented through direct effects. Finally, modeling transmission dynamics requires variables that are difficult, if not impossible, to observe, and assumptions about how infected and uninfected children mix are generally either unrealistic or unsupported by direct evidence.

The analysis proceeds from a government perspective, which will tend to underestimate the costs saved and to overestimate the cost per DALY. A more complete and satisfactory analysis would include benefits to the wider population. However, these data are not readily available in Pakistan without a special study.

## 2.2 Results of the Cost-effectiveness Analysis of New Vaccines in Pakistan

Table 4 presents the discounted results for the baseline cost-effectiveness analysis. Almost all the impact on burden of disease is attributable to preventing deaths rather than nonfatal episodes. The number of DALYs gained through vaccination with PCV and Hib vaccine are similar (3 million and 2.87 million, respectively), [13] but the number of DALYs gained associated with RV vaccination is 45 percent lower (1.65 million). [14]

[12] The WHO Guide for Economic Evaluations of Immunization Programmes (2009) recommends static model analysis if possible.

[13] Comparing Hib vaccine with PCV in more detail, the burden of meningitis prevented was greater for Hib, but this was balanced by the greater burden of pneumonia and invasive non-pneumonia-non-meningitis prevented by PCV. The efficacies against vaccine serotypes were comparable, but the overall impact of PCV was reduced by its incomplete serotype coverage and serotype replacement.

[14] Undiscounted, the total numbers of under-5 deaths avoided over the 10 birth cohorts were as follows: pneumococcal vaccine about 10,300 per year, Hib vaccine about 9,500, and rotavirus vaccine about 5,700.

**Table 3. Results of Baseline Cost-effectiveness Analysis of New Vaccines in Pakistan (2010-19)**

| Indicator | Hib Vaccine | PCV-10 | RV |
|---|---|---|---|
| DALYs Gained (000s) | 2,873 | 3,003 | 1,655 |
| Vaccination Costs ($ millions) | 182 | 763 | 439 |
| Treatment Savings ($ millions) | 118 | 88 | 106 |
| Cost/DALY ($ millions) | 22 | 225 | 201 |

*Source*: authors' calculations.

From the model, vaccination with PCV would be more than four times more expensive than Hib vaccination in Pakistan ($763 million compared to $182 million). The cost of RV vaccination in Pakistan would be in-between the other two options ($439 million). The levels of health care "savings" were broadly similar across the three vaccines. Table 4 shows that Hib vaccine in pentavalent form was the most cost-effective option at $22/DALY. The incremental cost-effectiveness ratios for PCV and RV vaccination in Pakistan are similar ($225/DALY and $201/DALY, respectively).

According to WHO, an intervention with a cost-effectiveness ratio less than the national GDP per capita for each DALY gained should be considered highly cost–effective.[15] The GDP per capita in Pakistan in 2008 was US$2,335 (World Bank, 2009). According to this standard, the results suggest that, Hib, pneumococcal and rotavirus vaccines are all highly cost-effective investments for Pakistan.

## 2.3 Scenario and sensitivity analysis of cost-effectiveness results

In the cost-effectiveness analysis, there are substantial uncertainties for most of the parameter estimates. The study attempted to reduce these uncertainties through a Delphi exercise. The scenario analysis produced a wide range of cost-effectiveness ratios for each vaccine. The favorable scenario incorporated high values for burden of disease, vaccine efficacy, serotype coverage, and health care costs avoided, with the unfavorable scenario being low in all respects. Table 5 shows that, regardless of the scenario, the three vaccines are still cost-effective options for Pakistan. Hib vaccine still remains the most cost-effective option of the three vaccines.

**Table 4. Relative Cost-effectiveness of Scenarios for New Vaccine Introduction in Pakistan**

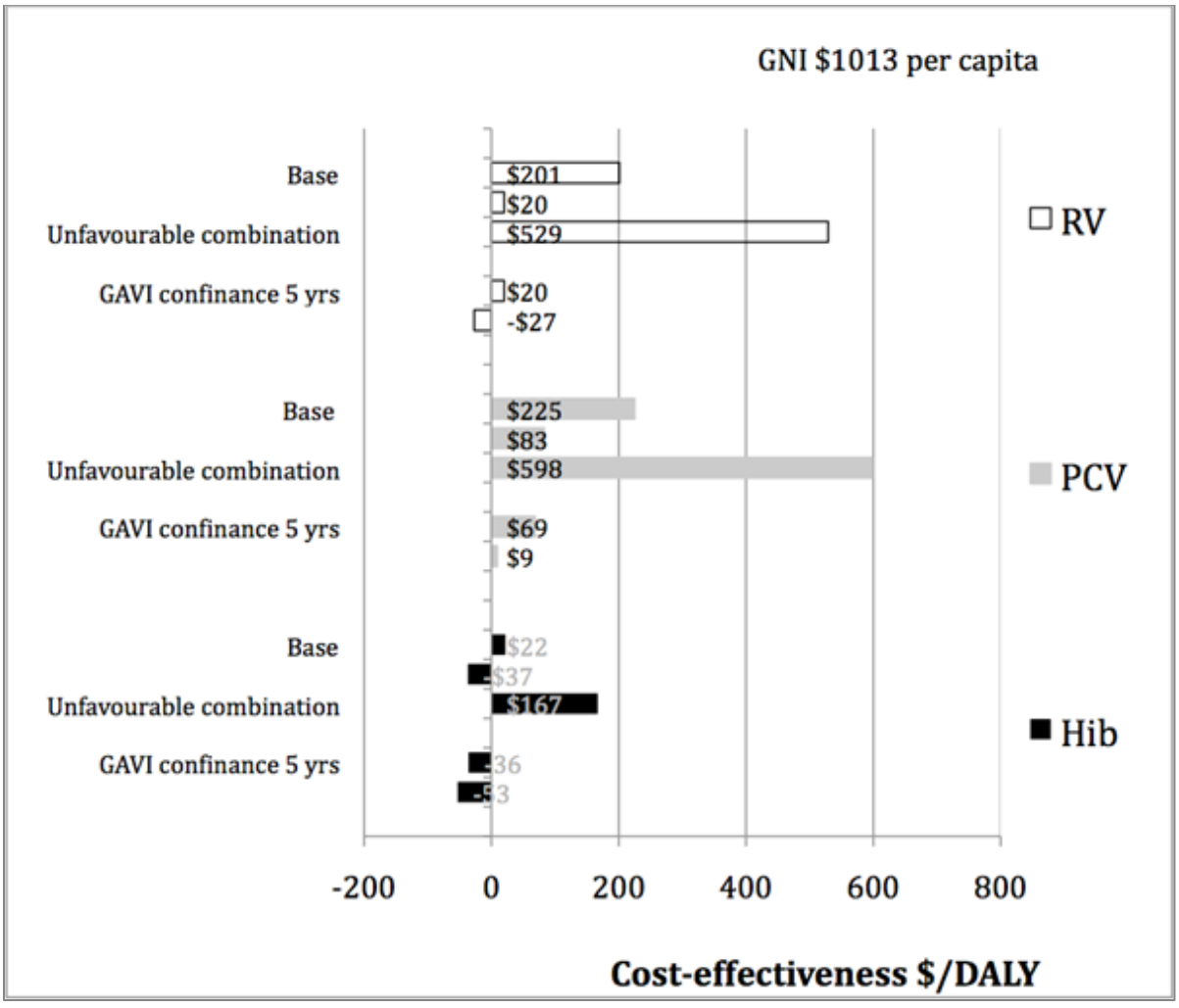
| New Vaccine | Baseline | Favorable scenario | Unfavorable scenario | Cofinance for 8 years | Co-finance for 5 years |
|---|---|---|---|---|---|
| Hib vaccine ($) | 22 | -37 | 167 | -53 | -36 |
| PCV-10 ($) | 225 | 83 | 598 | 9 | 69 |
| RotaTeq, 3 dose ($) | 201 | 20 | 529 | -27 | 20 |

Source: authors' calculations.

[15] Interventions costing less than three times the national GDP per capita are considered 'cost-effective'.

Figure 4 summarizes the results of selected scenario analyses. In the favorable scenarios, the most optimistic values for different parameters were bundled together, including lower demographic and disease burden projections; lower price trajectories for each vaccine; high vaccine efficacy; high health care utilization rates; and, high health care unit costs. The unfavorable scenarios bundled the least optimistic parameter values together. Additional scenarios varied the duration of GAVI co-financing, which varied from zero years (baseline) to five and eight years. In all cases, the three vaccines are found to be cost-effective, with a clear advantage to the Hib vaccine. Sensitivities to specific parameter scenarios and a probabilistic sensitivity analysis can be found in annex 4.

**Figure 4. Costs/DALY for Hib, PCV, and RV in Pakistan Under Selected Scenarios**




*Source*: authors' calculations.

# PART III: ANALYSIS OF FINANCIAL REQUIREMENTS FOR NEW VACCINE INTRODUCTION IN PAKISTAN

The purpose of the financial impact analysis was to estimate the total resource requirements to the GOP of introducing each new vaccine separately and in combination, and to compare the cost requirements with available government resources.

## 3.1 Methods

The analysis of financial implications of new vaccines had two components. First, an evaluation was made of the future payments for vaccines and freight. Second, the cost of additional cold chain requirements for each new vaccine was incorporated into the analysis. Estimation of cold chain costs is often lacking in national planning and for this reason, was important to include in this study.

### *3.1.1 Financial requirements*

The financial requirements focused on unit prices of vaccines, the co-financing requirement to be fulfilled by the GOP, and vaccine wastage rates. Vaccine prices were based on weighted average prices and related freight cost provided by the UNICEF Supply Division and from GAVI Alliance. Unit prices and co-financing rates for the financial analysis were the same as those used in the cost-effectiveness analysis. The unit price for the pentavalent vaccine was $3.60 per dose in 2009, with the five- and eight-year support periods extending to 2013 and 2016, respectively. Under the initial GAVI Alliance Co-Financing Policy, the GOP will be required to procure a share of each new vaccine at a price per dose of at least US$0.30-$0.40 for the first vaccine (pentavalent in this case) and at least US$0.15-$0.20 per dose for second and third new vaccines (GAVI Alliance, 2010). The purpose of co-financing is to increase country ownership and prepare the way for greater financial sustainability of new vaccines.

An Excel-based spreadsheet was constructed that incorporated various assumptions regarding population projections, vaccine wastage rates, duration of GAVI Alliance assistance, and year of introduction of new vaccines (single and in combination). Annex 3 sets out the parameters for each scenario in the analysis. S1 is the baseline scenario.[16] For PCV-10 and rotavirus vaccine, the analysis assumed a gap of two years between introduction of each vaccine. So if one vaccine was introduced in 2010, the other was assumed to be introduced in 2012, and vice versa.

Results for financial requirements were compared to projected national immunization expenditures, government health expenditures (GHE), and gross domestic product (GDP). Data on the national immunization budget and expenditures were obtained from the EPI Department. Government health expenditure data for Pakistan were based on estimates in the National Health Accounts (NHA) database of WHO (http://www.who.int/nha/en/), and GDP total and growth

[16] See also Sanderson, et al, 2010, Volume 2, Sections 9 and 10 for more details on the methods.

rates were based on World Bank Development Indicators (http://data.worldbank.org/data-catalog/world-development-indicators).

### *3.1.2 Analysis of cold chain requirements and costs for new vaccine introduction*

The financial analysis included estimates of national and sub-national cold chain requirements[17] associated with introduction of the new vaccines. Typically the cold chain includes cold stores (usually at central level), supported by freezers and ice-lined refrigerators, cold boxes, and vaccine carriers at various levels of the health system. Cold chain replacement in Pakistan has been irregular; equipment is replaced as it becomes unserviceable. Information about the status of the cold chain is incomplete and inconsistent; the last comprehensive inventory took place in 2003. For this analysis, data maintained by the national EPI was used as the basis of estimating additional cold chain needs.

**Table 5. Estimated Cold Chain Capacity in Pakistan in 2009**

| Item | Number (according to the national EPI) | Number (according to the cMYP) |
|---|---|---|
| Cold Room | 41 | 63 |
| Deep Freezer | 1,001 | 1,153 |
| ILR | 3,512 | 5,693 |
| Refrigerator | 3,382 | 422 |
| Solar Refrigerator | 47 | 5 |
| Cold box | 1,951 | 4,113 |
| Vaccine carrier | 59,352 | 6,894 |

*Source*: Ministry of Health, National EPI Program.

Both PCV-10 and RV vaccines come in single-dose packaging that will substantially affect the cold storage requirements needed for these vaccines. The period of analysis was from 2010 to 2020. Additional cold chain requirements were based on packed volume of new vaccines derived from the Vaccine Volume Calculator: http://www.who.int/immunization_delivery/systems_policy/logistics/en/index4.html.

Prices for cold chain equipment were obtained from the WHO. For cold chain rooms the analysis included the purchase price, delivery, and installation cost, and for smaller equipment (fridges

[17] The cold chain is a temperature-controlled supply chain that ensures the efficacy of vaccines.

and freezers) only the purchase price was considered.[18] Service life for cold chain equipment was assumed to be 10 years for refrigerators and freezers, and 15 years for cold rooms. Storage capacity figures for all types of equipment are those recommended by WHO. Thus, for example, the storage capacity of the 40 $m^3$ walk-in cold room was taken to be 9.5 $m^3$. Capacities of ice-lined refrigerators were taken from manufacturers' specifications.

A "volume efficiency factor" was taken into account in the analysis. Given that cold chain equipment is available in a limited range of sizes, the needs for cold chain storage at sub-national level are difficult to match. For the analysis, it was assumed that fridges and freezers use 80 percent of their capacity and cold rooms at Provincial Level use 90 percent of their capacity. The analysis also assumed that vaccines are stored at health facility/ vaccination point/ point of use, supported by a district store with capacity for at least one month of district requirements. While no assumption was made for volume efficiency at the national level, it was assumed that a 25 percent buffer stock of vaccines had to be maintained in order to even out irregularities in supply.

## 3.2 Results of the Financial Analysis of New Vaccine Introduction in Pakistan

This section explores the financial and cold chain requirements for introducing these vaccines, singly and in combination, to ascertain the overall affordability of these options to the GOP.

### *3.2.1 Financial requirements for new vaccines in Pakistan*

Financing the EPI in Pakistan has been a challenge for some time. Table 6 shows that in recent years the government has been disbursing an increasing amount of EPI budget per year, from 21 percent to 68 percent in 2006/07. In 2007/08, 133 percent of the budget requirement was disbursed, presumably related to procurement of pentavalent vaccine. At an exchange rate of 60.83 rupees per USD, disbursements reached $34.4 million in that year.

**Table 6: Trends in Budget Allocation for the EPI in Pakistan (Million Rupees)**

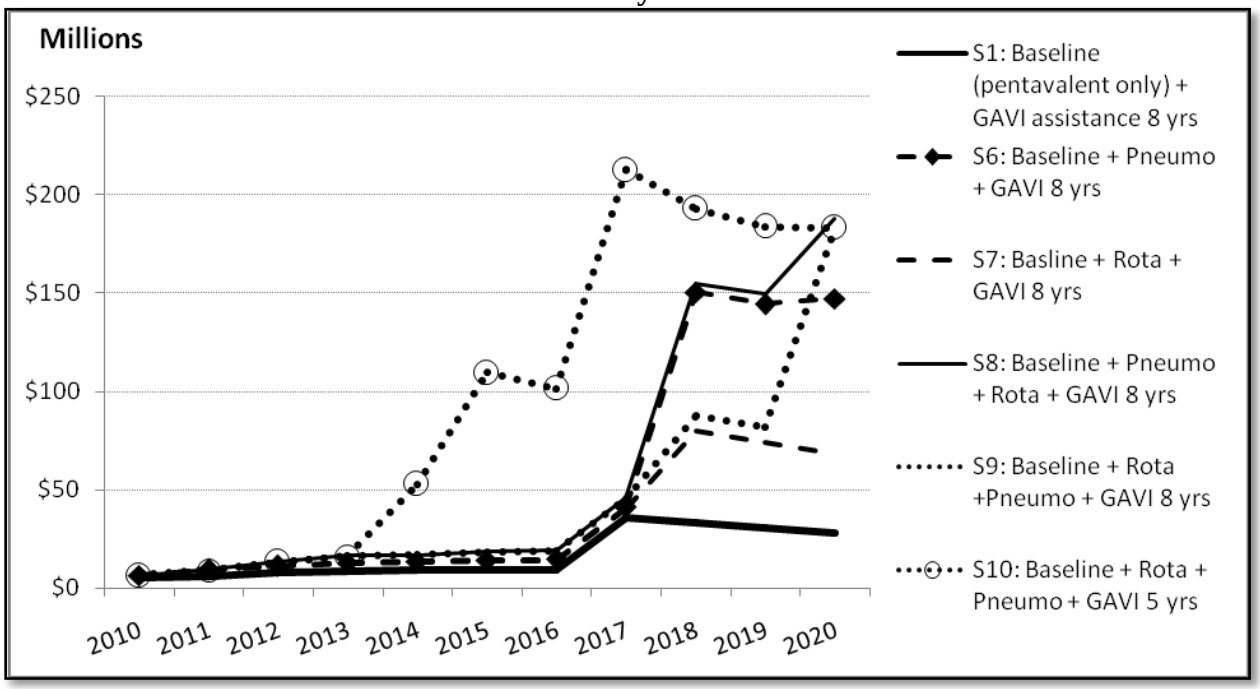
| Indicator | 2003-04 | 2004-05 | 2005-06 | 2006-07 | 2007-08 |
|---|---|---|---|---|---|
| EPI Budget Requirement | 957.3 | 1,477.2 | 1,604 | 1,758 | 1,577 |
| EPI Budget Allocation | 400 | 800 | 985 | 1,200 | 2,092 |
| Released Budget | 200 | 800 | 985 | 1,200 | 2,092 |
| Vaccine | 152 | 534 | 552 | 486 | 1,759 |
| Syringes | 0 | 0 | 200 | 0 | 124 |
| Transport and federal salaries | 48 | 266 | 233 | 714 | 209 |
| Release/requirement (percent) | 21 | 54 | 61 | 68 | 133 |

*Sources*: EPI Project Document PC-1 and Ministry of Finance, Government of Pakistan

[18] To provide for flexibility of cold chain storage capacity, it was assumed that all newly purchased cold rooms will be able to provide both negative and positive storage capacity by switching storage regimes. To assure the quality of storage capacity on the district level, it was assumed that all new purchases would be specialized ice-lined refrigerators.

From the analysis, the critical factors determining the level and timing of the financial requirement are the estimated vaccine price trajectories, particularly of PCV-10, and the duration of support from the GAVI Alliance. Annex 6 contains details of the results.

**Figure 5. Expected Cost per Year of New Vaccine Introduction in Pakistan by Scenario**




*Source*: authors' calculations.

Figure 5 shows that if the pentavalent vaccine were the only new vaccine introduced, and if the GAVI Alliance were to provide assistance for eight years, the total budget would rise from about $9.4m in 2016, to $36m in 2017, and decline to $28m in 2020, as the unit price of the vaccine declines. If GAVI assistance were to last only five years, the financial requirement would increase to $45m in 2014.

The financial requirement for PCV-10 and the pentavalent vaccine with eight years of GAVI support is greater, rising to $150m in 2018. The financial requirement for RV and pentavalent vaccines will be half of that ($80m) in the same year. However, the most costly scenario occurs when both PCV and RV are introduced in addition to the pentavalent vaccine, and GAVI support is limited to five years. In this case, the cost to the GOP for these two vaccines will be $213 million in 2017, up from an initial requirement of $16m in 2013. To put these figures into perspective, these requirements represent an increase of 520 percent over total immunization program disbursements in 2007/08, and 637 percent more than total vaccine disbursements for the same year.

Reducing the wastage rate of the pentavalent vaccine from the 10 percent estimated in the National Comprehensive Multi-Year Plan (cMYP) to the 5 percent recommended by the GAVI Alliance would save $1.7m per year during the period 2017 to 2020.

### *3.2.2 Cold chain requirements and costs*

Regardless of the scenario evaluated, investments in cold chain development and maintenance would represent value for money in Pakistan. Table 7 shows that for pentavalent vaccine alone, an initial investment of about $300,000 followed by expenditures of $50,000-$100,000 per year would reduce vaccine wastage from 10 percent to 5 percent and potentially result in annual cost savings of $2m. With the introduction of additional vaccines, savings from reduced wastage would be even greater. The increase over baseline is greater than for pneumococcal because the oral vaccine is much bulkier.[19] Cold chain requirements reach their peak in 2019 in the scenario of introducing pentavalent, PCV-10 and then RV to $737,000. Cold chain requirements increase in 2011 and after 2017, when a substantial number of District-level ice-lined refrigerators will need to be replaced. With fewer but larger deliveries of vaccines at the national level, the need for cold chain storage capacity will increase to $856,000 per year in 2010. [20]

**Table 7. Comparison of Cold Chain Cost Requirements (current $000's USD) by Major Scenario and Year**

| Year/ Vaccine | Pentavalent Alone | Penta + PCV-10 | Penta + RV | Penta, RV, PCV-10 | Penta, PCV-10, RV |
|---|---|---|---|---|---|
| **Duration of GAVI Support** | **8 Years** | **8 Years** | **8 Years** | **8 Years** | **8 Years** |
| 2010 | 311.1 | 350.0 | 427.8 | 427.8 | 350.0 |
| 2011 | 38.9 | 116.7 | 505.5 | 505.5 | 116.7 |
| 2012 | 77.8 | 77.8 | 116.7 | 233.3 | 505.5 |
| 2013 | 77.8 | 77.8 | 194.4 | 311.1 | 466.7 |
| 2014 | 38.9 | 194.4 | 155.6 | 194.4 | 155.6 |
| 2015 | 77.8 | 155.6 | 155.6 | 199.9 | 194.4 |
| 2016 | 194.4 | 77.8 | 194.4 | 704.8 | 635.5 |
| 2017 | 77.8 | 155.6 | 548.3 | 668.5 | 665.2 |
| 2018 | 116.7 | 116.7 | 579.1 | 646.2 | 676.2 |
| 2019 | 116.7 | 142.0 | 626.7 | 737.1 | 688.3 |
| 2020 | 116.7 | 233.3 | 350.0 | 350.0 | 350.0 |

*Source:* authors' calculations.

Whatever decisions are made about adding new vaccines to the national immunization program, the cold chain investments required would be less than $1million per year, and in most years under $500,000. This is small compared to the commitments involved in vaccine purchase, which even during the co-financing period are of the order of $10-$20m. The case for investment in cold chain infrastructure in Pakistan represents a good return on investment.

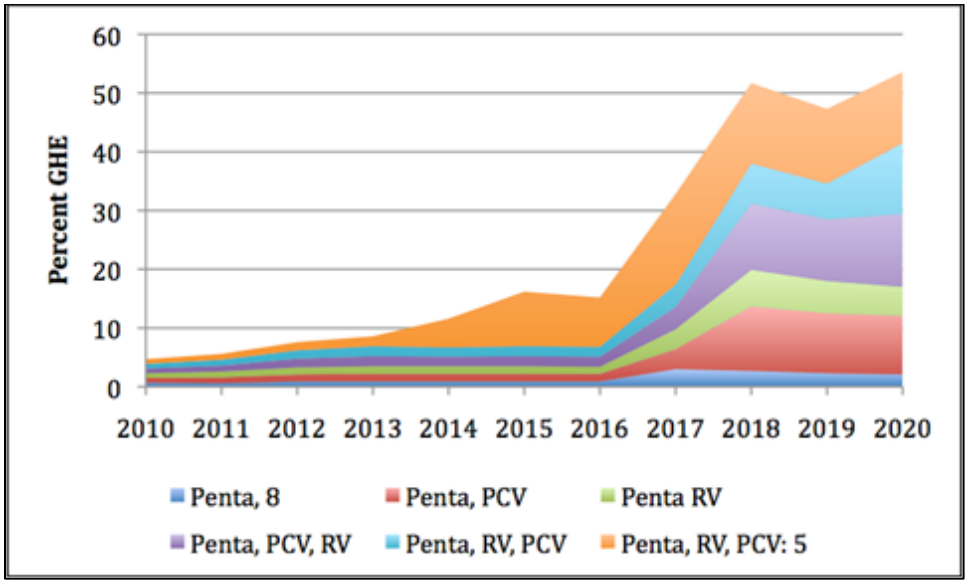
[19] The packed volume of one dose of Rotavirus vaccine is 17.1 ml. Pack volume of one dose of Pneumococcal (PCV10) vaccine is 4.8 ml.

[20] Note that changes in transportation and delivery costs are not factored into this analysis, so that the results represent conservative estimates.

### *3.2.3 Summary of financial requirements and comparison to GOP resources*

Figure 6 summarizes the financial implications of the co-financing requirements of new vaccines during GAVI support; costs of new vaccines after GAVI support ends; and, cold chain requirements throughout. The total cost requirement of new vaccines peaks in 2017 for pentavalent vaccine ($36m); in 2018 for pentavalent and pneumococcal vaccines ($150m); in 2020 for pentavalent, pneumococcal, and rotavirus vaccines together ($188m); and in 2017 for the three new vaccines together if GAVI assistance is for 5 rather than eight years ($213m).

**Figure 6. Financial Requirements of New Vaccines Compared to Government Health Expenditures by Year (percent)**




*Source:* authors' calculations.

Total financial requirements per year are compared to projections of total immunization expenditures and GHE. [21] Introducing pentavalent, PCV-10, and RV vaccines with GAVI support for five years would account for 40 percent of national immunization expenditures, and 15 percent of government health expenditures. However, financial requirements would still be less than 0.1 percent of GDP.

These data suggest that introducing all three vaccines to the national immunization program in Pakistan will present serious financial challenges for the GOP unless overall health spending

[21] Projections of total immunization expenditures were based on the 3-year average growth rate of expenditures reported by the national EPI of Pakistan. For the analysis, it was assumed that the share of GHE to GDP remained constant over the study period. GDP was projected to grow by 7 percent per year based on historical trends.

increases. In addition, while vaccines are generally cost-effective, there may be other priority health programs worth financing by the government. Therefore, prior to introduction of new vaccines in Pakistan, careful consideration needs to be given to how they will be financed after GAVI support ends.

## Part IV: Discussion

This study suggests that all three vaccines would be highly cost-effective in Pakistan using the WHO-CHOICE threshold of GDP/capita as guidance. PCV would have the greatest impact at about 10,300 deaths avoided per year, followed closely by Hib vaccine at about 9,500, and RV with 5,700 deaths prevented. However, vaccine price is a critical determinant of cost-effectiveness. PCV and RV offer comparable value for money, but Hib vaccine would be a more cost-effective choice.

The cost-effectiveness results are within the range of estimates found in other studies. For instance, Niessen et al (2006) estimated cost-effectiveness ratios for eight interventions designed to reduce the burden of childhood pneumonia. In the Eastern Mediterranean Region D, which includes Pakistan, they ranked zinc supplementation and breast-feeding promotion first and second respectively, and Hib vaccination was third at $35 to $54 per DALYS, and pneumococcal 6$^{th}$ at $50 to $223: all comparable ranges to ours. In the Disease Control Priorities Project the most cost effective intervention of those considered for diarrhea in South Asia was ORS (US$642 per DALY). A two-dose rotavirus vaccine was shown to be cost-effective in Vietnam (Fischer et al., 2005). The cost/DALY prevented ranged from $40 to $192 and the cost per life saved varied from $1,330 to $6,382, depending on the vaccine price used ($1 to $20 per dose). In China, a study estimated the cost per case prevented of rotavirus at $0.80 (societal perspective) and $19.70 (patient perspective).

Regardless of their cost-effectiveness, the GOP will need to find the resources to finance and sustain the use of these vaccines beyond the period of initial support from the GAVI Alliance. The study found that the budgetary requirement of annual investments in the cold chain would be relatively modest with an excellent return. However if external support for the EPI budget were to come to an end before substantial falls in vaccine price, introducing these vaccines would mean a sharp increase in the GOP's financial obligations to the national vaccination program.

If external support for vaccine purchase were to come to an end before substantial falls in vaccine price, introducing these vaccines would require a sharp increase in government health expenditure (GHE). However in recent years, GHE has been growing by 7 percent to 8percent per year. If this continues, GHE would reach about US$100M, which is less than half the cost of the three new vaccines. Assuming the increased GHE is not allocated to other health priorities, the GOP could "afford" pentavalent vaccine, and possibly a phased-in approach to PCV-10.

In 2010, GHE was approximately 0.5 percent of GDP, which by international standards is very low. [22] The governments of 47 countries with lower per capita income spent a median of I$23 per capita per year on health compared to Pakistan's I$9. Even if government health expenditure in Pakistan were to grow steadily at 10 percent per year, and GDP grew at only 3 percent, by 2020 government health expenditure would be around 1 percent of GDP, still well under the 2 percent for health spent elsewhere and envisaged in Pakistan's Fiscal Responsibility Act. All this suggests that even though introducing PCV-10 and RV would involve a sharp

[22] According to the WHO statistical information system the median for the 47 countries with GNI per capita *less* than Pakistan's (using the international $, which is adjusted for purchasing power parities) was 8.4 percent.

increase in the financial requirements for vaccination, financing the full cost of these vaccines will require government prioritization of health and vaccination.

With support from the GAVI Alliance, the country does not bear any risk associated with vaccine price fluctuations for at least five to eight years, and the GoP's budget obligations can be estimated with reasonable confidence. However, there are other factors that affect the government's financial contribution, such as the accuracy of population projections, vaccine wastage rates and effective vaccination coverage rates. While the "grace" period will help to cushion these risks, it would be in the country's best interests to develop strategies, skills, and procedures for strengthening procurement, vaccine management, and managing price uncertainty in the longer term.

One of the arguments in favor of spending on vaccination programs has been that they are more equitably distributed than treatment services. However, the evidence on this from Pakistan is at best equivocal. Concentration indexes (ConIs) were calculated from data on the use of health care by wealth quintiles in the Pakistan Demographic and Health Survey for 2006/7, with 0 percent as perfect equity and 100 percent as maximum inequity. Although vaccination (ConI 8 percent for BCG, 10 percent for first dose of DTP) was much more equitable than maternity care (30 percent for assistance by a skilled provider), it is slightly less equitable than the use of basic treatment services for acute respiratory infection (8 percent for those seen at a health facility, 8 percent antibiotics) and treatment of diarrhea (7 percent for those seen at a health facility, 3 percent for oral rehydration therapy). This is concerning because data from the PDHS suggest that death rates in children aged under 5 were almost three times as high in the bottom wealth quintile as in the top two. In this respect, the higher the risk of mortality, the lower the chance of being vaccinated. Unless this inequity is addressed in Pakistan, much of the potential benefit from the new vaccines will be lost. The analysis did show that the relatively high coverage rates for polio vaccination in Pakistan were associated with high levels of equity (ConI: 2 percent for 1$^{st}$ and 3$^{rd}$ doses).

One issue that was not addressed in this analysis is the possibility of a more targeted vaccination program. If the government is unable to introduce pneumococcal and rotavirus vaccines at the same time, it could consider introducing at least one of them initially in selected areas with the highest mortality, and gradually phasing in the new vaccine to other geographic areas.

Data are always an issue for exercises of this kind, particularly in lower-income countries. Data on patterns of health care utilization and health care unit costs are particularly challenging to obtain in Pakistan. Fortunately the results were not sensitive to these parameters, partly because this analysis was from a government perspective and only about 10 percent of health care is funded, directly by the government; and, partly because per patient health care costs in Pakistan are relatively modest. Doubling the government health care costs avoided made a difference to the ICERs of only about $30/DALY.

This exercise has demonstrated that an assessment of the relative cost-effectiveness of new vaccines using an Excel-based model can be undertaken for a low-income country such as Pakistan. Pairing the cost-effectiveness analysis with an assessment of the long-term financial

obligations to sustain new vaccines in the population provides a comprehensive view for decision makers.

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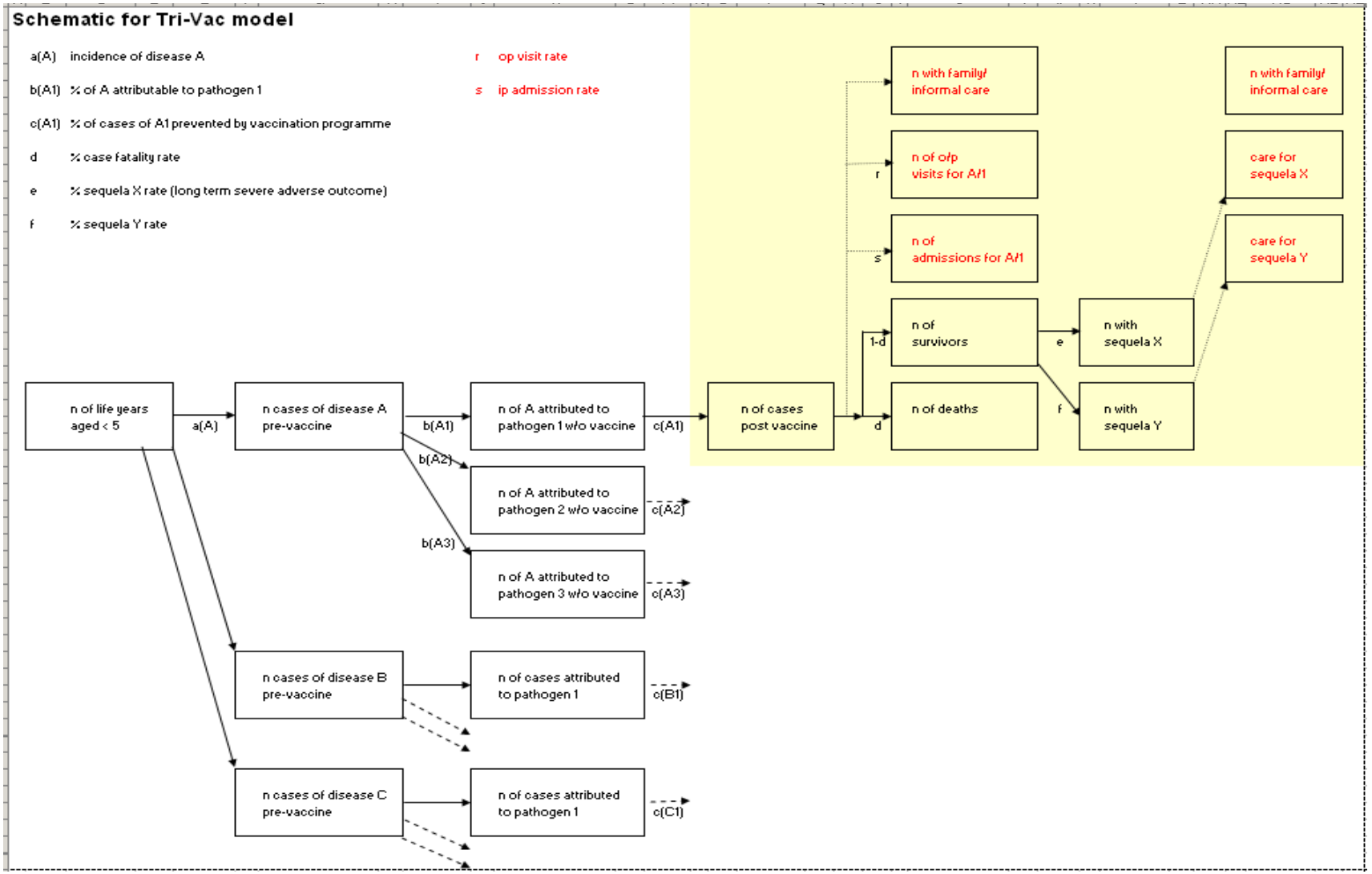
# ANNEXES

## Annex 1: Schematic for the TriVac/ProVac Model



# Annex 2: Baseline (mid) and Scenario (low and high) Model Parameter Values

| Infection | Disease | Variant | Burden | | | | Efficacy | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Incidence /100,000 | % case fatality ratio | % of survivors with any major sequela | % of survivors with multiple major sequelae | Full schedule | 1 dose [1] | 2 doses [1] | Serotype coverage |
| Hib | Pneumonia | Mid | 2,010 | 2.7 percent | | | 95 percent | 60 percent | 95 percent | 100 percent |
| | | Low | 1,835 | 1.9 percent | | | 60 percent | 0 percent | 34 percent | 100 percent |
| | | High | 3,284 | 3.1 percent | | | 99 percent | 86 percent | 99 percent | 100 percent |
| | Meningitis | Mid | 27.5 | 30 percent | 10 percent | 20 percent | 95 percent | 60 percent | 95 percent | 100 percent |
| | | Low | 16.3 | 20 percent | 7 percent | 20 percent | 60 percent | 0 percent | 34 percent | 100 percent |
| | | High | 38.3 | 40 percent | 15 percent | 20 percent | 99 percent | 86 percent | 99 percent | 100 percent |
| | Invasive NPNM | Mid | 4.2 | 1.0 percent | | | 80 percent | 60 percent | 95 percent | 100 percent |
| | | Low | 2.5 | 1.0 percent | | | 60 percent | 0 percent | 34 percent | 100 percent |
| | | High | 5.9 | 1.0 percent | | | 90 percent | 86 percent | 99 percent | 100 percent |
| Pneumococcal | Otitis media | Mid | 54,000 | 0 percent | | | 60 percent | 60 percent | 60 percent | 70 percent |
| | | Low | 45,000 | 0 percent | | | 40 percent | 40 percent | 60 percent | 55 percent |
| | | High | 63,000 | 0 percent | | | 90 percent | 80 percent | 99 percent | 75 percent |
| | Pneumonia | Mid | 3,250 | 3.7 percent | | | 89 percent | | | 70 percent |
| | | Low | 2,529 | 3.2 percent | | | 75 percent | | | 55 percent |
| | | High | 4,044 | 5.0 percent | | | 96 percent | | | 75 percent |
| | Meningitis | Mid | 14 | 40 percent | 25 percent | 10 percent | 89 percent | | | 70 percent |
| | | Low | 11.6 | 30 percent | 15 percent | 5 percent | 75 percent | | | 55 percent |
| | | High | 15.9 | 50 percent | 35 percent | 15 percent | 96 percent | | | 75 percent |
| | Invasive NPNM | Mid | 69.3 | 3.2 percent | | | 89 percent | | | 70 percent |
| | | Low | 57.6 | 2.5 percent | | | 75 percent | | | 55 percent |
| | | High | 78.7 | 3.8 percent | | | 96 percent | | | 75 percent |
| Rotavirus | Non-severe diarrhoea | Mid | 43,200 | 0 percent | | | 45 percent | 60 percent | 80 percent | 100 percent |
| | | Low | 28,800 | 0 percent | | | 35 percent | 50 percent | 70 percent | 100 percent |
| | | High | 57,600 | 0 percent | | | 55 percent | 70 percent | 90 percent | 100 percent |
| | Severe diarrhoea | Mid | 9,600 | 0.8 percent | | | 50 percent | 60 percent | 80 percent | 100 percent |
| | | Low | 8,000 | 0.5 percent | | | 40 percent | 50 percent | 70 percent | 100 percent |
| | | High | 11,200 | 1.2 percent | | | 60 percent | 70 percent | 90 percent | 100 percent |

Key: 1: With reduced schedule, percent of efficacy of full schedule

## Annex 3: Results of the Sensitivity Analysis for the Cost-effectiveness Exercise of New Vaccines in Pakistan

| | | Hib | | | | PCV | | | | RV | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *DALYs gained (1000s)* | *Vaccination costs ($million)* | *Treatment savings ($million)* | *$Cost/ DALY* | *DALYs gained (1000s)* | *Vaccination costs ($million)* | *Treatment savings ($million)* | *$Cost/ DALY* | *DALYs gained (1000s)* | *Vaccination costs ($million)* | *Treatment savings ($million)* | *$Cost/ DALY* |
| **Base case** | | 2,873 | $182 | $118 | $22 | 3,003 | $763 | $88 | $225 | 1,655 | $439 | $106 | $201 |
| Population projection | High estimate [1] | 3,721 | $231 | $154 | $21 | 3,857 | $985 | $113 | $226 | 2,144 | $562 | $137 | $198 |
| Disease burden | High estimate [1] | 5,346 | $182 | $186 | -$1 | 4,989 | $763 | $108 | $131 | 2,890 | $439 | $125 | $109 |
| | Low estimate [1] | 1,757 | $182 | $99 | $47 | 2,009 | $763 | $69 | $345 | 865 | $439 | $87 | $407 |
| Case fatality ratios | No improvement | 3,175 | $182 | $118 | $20 | 3,305 | $763 | $88 | $204 | 1,842 | $439 | $106 | $181 |
| Vaccination coverage | No improvement | 2,765 | $175 | $114 | $22 | 2,900 | $728 | $84 | $222 | 1,590 | $421 | $101 | $201 |
| Vaccine efficacy | High estimate [1] | 3,135 | $182 | $129 | $17 | 3,394 | $763 | $99 | $195 | 2,039 | $439 | $130 | $151 |
| | Low estimate [1] | 1,526 | $182 | $63 | $78 | 2,359 | $763 | $69 | $294 | 1,289 | $439 | $82 | $277 |
| Herd effect | 20% boost | 3,590 | $182 | $148 | $10 | 3,754 | $763 | $109 | $174 | 2,069 | $439 | $132 | $148 |
| Serotype replacement [2] | | 2,344 | $182 | $95 | $37 | 2,073 | $763 | $59 | $339 | 1,351 | $439 | $85 | $261 |
| Waning efficacy [3] | | 2,731 | $182 | $112 | $25 | 2,855 | $763 | $83 | $238 | 1,741 | $439 | $111 | $188 |
| Vaccine price trajectory | High estimate [1] | 2,873 | $205 | $118 | $30 | 3,003 | $813 | $88 | $241 | 1,655 | $466 | $106 | $218 |
| | Low estimate [1] | 2,873 | $171 | $118 | $19 | 3,003 | $731 | $88 | $214 | 1,655 | $422 | $106 | $191 |
| GAVI support | 8 years | 2,873 | -$35 | $118 | -$53 | 3,003 | $115 | $88 | $9 | 1,655 | $61 | $106 | -$27 |
| | 5 years | 2,873 | $13 | $118 | -$36 | 3,003 | $296 | $88 | $69 | 1,655 | $139 | $106 | $20 |
| Health care costs avoided | Up by 100% | 2,873 | $182 | $232 | -$18 | 3,003 | $763 | $174 | $196 | 1,655 | $439 | $211 | $137 |
| | Down by 50% | 2,873 | $182 | $59 | $43 | 3,003 | $763 | $44 | $239 | 1,655 | $439 | $53 | $233 |
| No discounting | | 7,857 | $200 | $138 | $8 | 8,105 | $863 | $101 | $94 | 4,506 | $489 | $124 | $81 |
| Favourable combination | | 5,834 | $182 | $401 | -$37 | 6,041 | $763 | $261 | $83 | 3,559 | $439 | $308 | $37 |
| Unfavourable combination | | 933 | $182 | $26 | $167 | 1,240 | $763 | $21 | $598 | 674 | $439 | $34 | $601 |

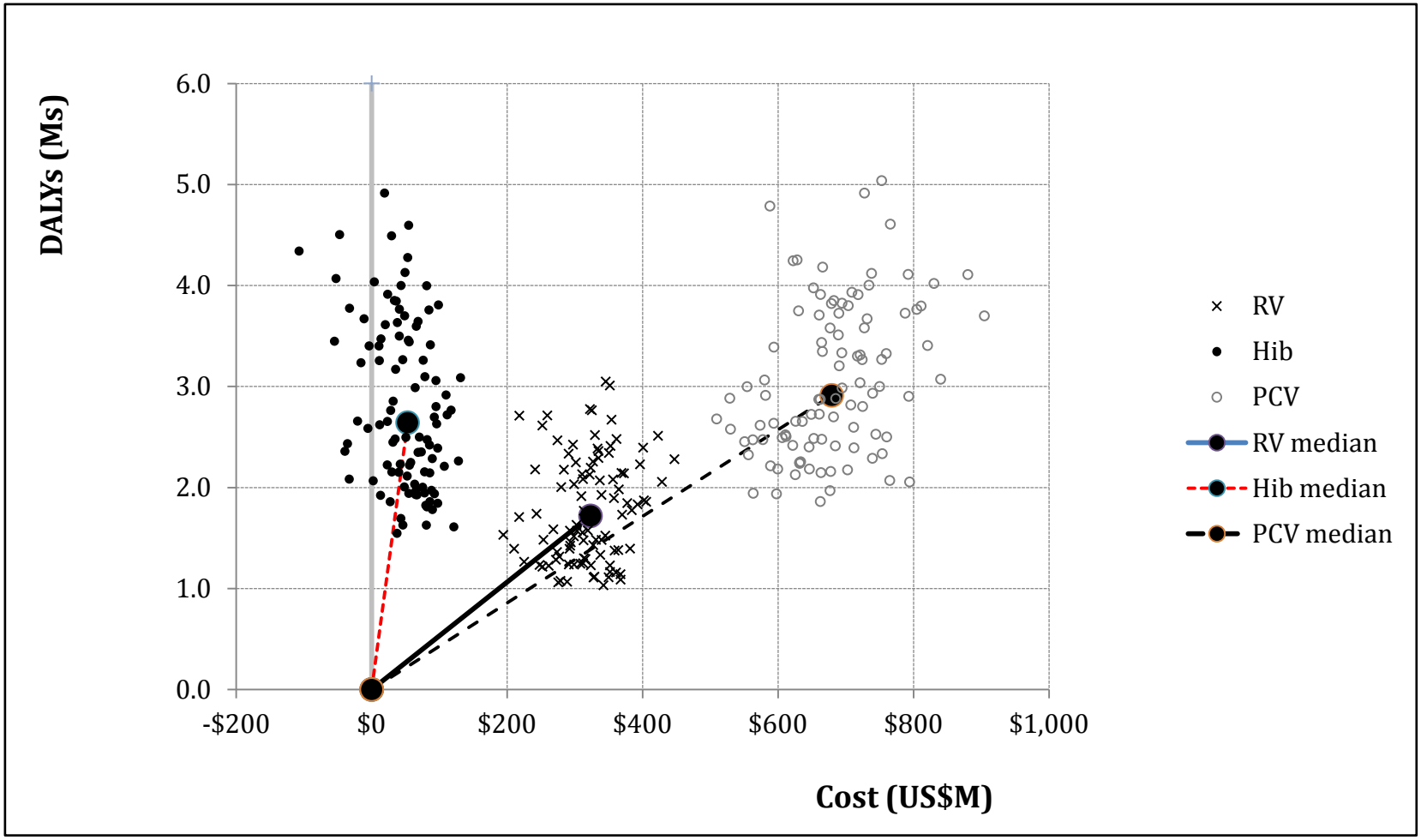
Key

*1. High and low estimates* see Table 2

*2. Serotype replacement* Baselines 0% per year for Hib and RV, 5% for PCV Variants 5% per year for Hib and RV, 15% for PCV.

*3. Waning efficacy* Baselines 0% per year for Hib and PCV, 5% for RV Variants for 5% Hib and PCV, 0% for RV.

**Annex 4: Probabilistic Sensitivity Analysis of the Cost-effectiveness of Hib, PCV, and RV vaccines**



## Annex 5: Scenarios for the Financial Sustainability Analysis

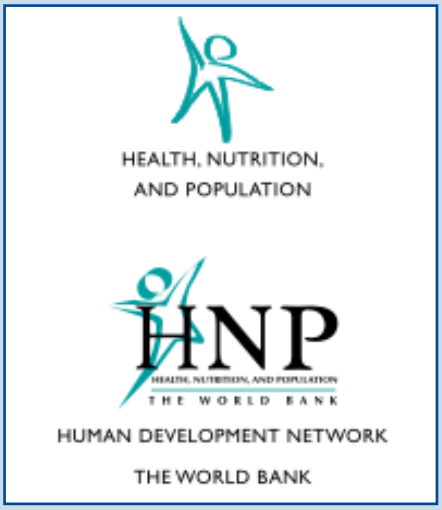
| *Scenario* | *Element* | *Value* |
|---|---|---|
| *S1* | *Pentavalent* vaccine introduced in:<br>Target group coverage in consecutive years<br>Target group numbers:<br>Duration of GAVI assistance:<br>Vaccine wastage rates:<br>Vaccine prices:<br>Vaccine buffer stock requirements:<br>Vaccine deliveries at National level:<br>Vaccine deliveries at Provincial/ District levels:<br>Cold room usable life:<br>Fridge & freezer usable life: | 2009<br>85 percent, 87 percent, 90 percent, 92 percent, 94 percent, 96 percent, ...<br>as per EPI births projections<br>8 years<br>GAVI recommended (5 percent for 1-dose vaccines)<br>GAVI recommended, projected to 2020<br>25 percent<br>4 per year<br>6 per year<br>15 years<br>10 years |
| *S2* | Duration of GAVI assistance: | 5 years, not 8 |
| *S3* | Target population group numbers | UN birth projections |
| *S4* | Vaccine deliveries at National level | 2 per year, not 4 |
| *S5* | Wastage rates for single-dose vaccines | 10 percent, not 5 percent |
| *S6* | *Pneumococcal* vaccine added from<br>coverage | 2010<br>25 percent in first year, then as per pentavalent |
| *S7* | *Rotavirus* vaccine added from<br>coverage | 2010<br>25 percent in first year, then as per pentavalent |
| *S8* | *Pneumococcal* vaccine added from<br>coverage<br>*Rotavirus* vaccine added from<br>coverage | 2010<br>25 percent, in first year, then as per pentavalent<br>2012<br>50 percent in first year, then as per pentavalent |
| *S9* | *Rotavirus* vaccine added from<br>coverage<br>*Pneumococcal* vaccine added from<br>coverage | 2010<br>50 percent in the first year, then as per pentavalent<br>2012<br>25 percent, in first year then as per pentavalent |

| | | |
|---|---|---|
| *S10* | *Rotavirus* vaccine added from<br>coverage<br>*Pneumococcal* vaccine added from<br>coverage<br>*and* duration of GAVI assistance | 2010<br>50 percent in the first year, then as per pentavalent<br>2012<br>25 percent, in first year, then as per pentavalent<br>5 years, not 8 |

## Annex 6: Estimated financial requirements for vaccine purchase and cold chain investment, 2010-2020

| | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***S1: Pentavalent alone; GAVI support 8 yrs*** | | | | | | | | | | | |
| Co-financing requirement ($1000s) | 5,425.6 | 5,697.5 | 8,083.8 | 8,455.5 | 8,863.8 | 9,287.6 | 9,482.2 | 36,051.9 | 33,111.3 | 30,410.5 | 27,930.0 |
| Cold chain investment ($1000s) | 311.1 | 38.9 | 77.8 | 77.8 | 38.9 | 77.8 | 194.4 | 77.8 | 116.7 | 116.7 | 116.7 |
| Total requirement as percent of EPI budget | 2.8% | 2.8% | 3.6% | 3.6% | 3.3% | 3.2% | 3.1% | 10.0% | 8.8% | 7.7% | 6.8% |
| Total requirement as percent of GoP health budget | 0.7% | 0.6% | 0.9% | 0.9% | 0.9% | 0.9% | 0.9% | 3.0% | 2.7% | 2.3% | 2.1% |
| **Total Financial Implications** | **5,736.7** | **5,736.3** | **8,161.5** | **8,533.2** | **8,902.7** | **9,365.4** | **9,676.7** | **36,129.6** | **33,227.9** | **30,527.2** | **28,046.7** |
| ***S6: Penta + Pneumo; GAVI support 8 yrs*** | | | | | | | | | | | |
| Co-financing requirement ($1000s) | 6,465.8 | 9,203.7 | 11,283.6 | 12,918.1 | 13,541.9 | 14,189.5 | 14,486.7 | 41,187.0 | 150,349.9 | 144,491.4 | 147,207.5 |
| Cold chain investment ($1000s) | 350.0 | 116.7 | 77.8 | 77.8 | 194.4 | 155.6 | 77.8 | 155.6 | 116.7 | 142.0 | 233.3 |
| Total requirement as percent of EPI budget | 3.4% | 4.5% | 4.9% | 5.4% | 5.0% | 4.8% | 4.6% | 11.3% | 30.3% | 28.3% | 27.6% |
| Total requirement as percent of GoP health budget | 0.8% | 1.0% | 1.2% | 1.3% | 1.3% | 1.3% | 1.3% | 3.4% | 11.0% | 10.2% | 10.0% |
| **Total Financial Implications** | **6,815.8** | **9,320.4** | **11,361.4** | **12,995.8** | **13,736.3** | **14,345.0** | **14,564.5** | **41,342.5** | **150,466.5** | **144,633.3** | **147,440.8** |
| ***S7: Penta + Rota; GAVI support 8 yrs*** | | | | | | | | | | | |
| Co-financing requirement ($1000s) | 6,411.0 | 9,019.2 | 11,115.2 | 12,569.6 | 13,085.3 | 13,619.4 | 13,927.0 | 40,612.7 | 79,869.7 | 73,971.6 | 68,512.5 |
| Cold chain investment ($1000s) | 427.8 | 505.5 | 116.7 | 194.4 | 155.6 | 155.6 | 194.4 | 548.3 | 579.1 | 626.7 | 350.0 |
| Total requirement as percent of EPI budget | 3.4% | 4.6% | 4.8% | 5.3% | 4.8% | 4.7% | 4.4% | 11.3% | 18.9% | 16.9% | 15.1% |
| Total requirement as pertcentof GoP health budget | 0.8% | 1.0% | 1.2% | 1.3% | 1.3% | 1.3% | 1.2% | 3.4% | 6.2% | 5.5% | 4.9% |
| **Total Financial Implications** | **6,838.8** | **9,524.7** | **11,231.8** | **12,764.1** | **13,240.9** | **13,774.9** | **14,121.5** | **41,160.9** | **80,448.7** | **74,598.4** | **68,862.4** |
| ***S8: Penta + Pneumo + Rota; GAVI support 8 yrs*** | | | | | | | | | | | |
| Co-financing requirement ($1000s) | 6,465.8 | 9,203.7 | 13,358.7 | 16,335.7 | 16,708.0 | 18,521.2 | 18,931.5 | 45,747.8 | 155,029.7 | 149,293.3 | 187,790.0 |
| Cold chain investment ($1000s) | 350.0 | 116.7 | 505.5 | 466.7 | 155.6 | 194.4 | 635.5 | 665.2 | 676.2 | 688.3 | 350.0 |
| Total requirement as percent of EPI budget | 3.4% | 4.5% | 5.9% | 6.9% | 6.1% | 6.2% | 6.1% | 12.5% | 31.1% | 29.0% | 32.7% |
| Total requirement as percent of GoP health budget | 0.8% | 1.0% | 1.5% | 1.7% | 1.6% | 1.7% | 1.7% | 3.8% | 11.3% | 10.5% | 12.4% |
| **Total Financial Implications** | **6,815.8** | **9,320.4** | **13,864.2** | **16,802.4** | **16,863.6** | **18,715.6** | **19,567.1** | **46,413.0** | **155,705.9** | **149,981.7** | **188,139.9** |
| ***S9: Penta + Rota +Pneumo; GAVI support 8 yrs*** | | | | | | | | | | | |
| Co-financing requirement ($1000s) | 6,411.0 | 9,019.2 | 13,305.5 | 16,290.7 | 16,637.7 | 18,503.8 | 18,915.1 | 45,730.9 | 87,926.8 | 81,944.5 | 183,040.6 |
| Cold chain investment ($1000s) | 427.8 | 505.5 | 233.3 | 311.1 | 194.4 | 199.9 | 704.8 | 668.5 | 646.2 | 737.1 | 350.0 |
| Total requirement as percent of EPI budget | 3.4% | 4.6% | 5.8% | 6.8% | 6.0% | 6.2% | 6.1% | 12.5% | 20.4% | 18.4% | 32.2% |
| Total requirement as percent of GoP health budget | 0.8% | 1.0% | 1.4% | 1.7% | 1.6% | 1.7% | 1.7% | 3.8% | 6.8% | 6.1% | 12.1% |
| **Total Financial Implications** | **6,838.8** | **9,524.7** | **13,538.9** | **16,601.8** | **16,832.2** | **18,703.8** | **19,619.9** | **46,399.4** | **88,572.9** | **82,681.6** | **183,390.6** |
| ***S10: Penta + Rota + Pneumo; GAVI support 5 yr*** | | | | | | | | | | | |
| Co-financing requirement ($1000s) | 6,411.0 | 9,019.2 | 13,305.5 | 16,290.7 | 52,757.6 | 109,522.7 | 101,411.3 | 212,590.6 | 192,898.1 | 183,826.5 | 183,040.6 |
| Cold chain investment ($1000s) | 427.8 | 505.5 | 233.3 | 311.1 | 194.4 | 199.9 | 704.8 | 668.5 | 646.2 | 737.1 | 350.0 |
| Total requirement as percent of EPI budget | 3.4% | 4.6% | 5.8% | 6.8% | 16.8% | 28.0% | 25.2% | 39.6% | 35.9% | 33.5% | 32.2% |
| Total requirement as percent of GoP health budget | 0.8% | 1.0% | 1.4% | 1.7% | 4.9% | 9.3% | 8.4% | 15.4% | 13.7% | 12.7% | 12.1% |
| **Total Financial Implications** | **6,838.8** | **9,524.7** | **13,538.9** | **16,601.8** | **52,952.0** | **109,722.7** | **102,116.2** | **213,259.1** | **193,544.3** | **184,563.6** | **183,390.6** |

*Source:* authors' calculation

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