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RESEARCH AND EVALUATION REPORT

Cost-effectiveness of an Intervention to Increase Immunization Coverage in Pakistan

NOVEMBER 2016

This evaluation report was prepared by University Research Co., LLC (URC) for review by the United States Agency for International Development (USAID) and authored by Edward Broughton of URC under the USAID Applying Science to Strengthen and Improve Systems (ASSIST) Project. The work of the USAID ASSIST Project is made possible by the generous support of the American people through USAID.

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Acknowledgements

The author thanks the staff at John Snow International in Pakistan, including Drs. Nabeela Ali, Arshad Mahmood, and Adnan Riaz, for providing data on their program implementation and for review of the draft report, and Monica Villanueva and Steve Anderson of the United States Agency for International Development (USAID) Mission in Pakistan for supporting this evaluation. The author acknowledges the reviews provided by Ms. Anne Austin of John Snow International; Ms. Lani Marquez of University Research Co., LLC (URC); and Dr. James Heiby of the USAID Office of Health Systems.

This report was prepared by URC under the USAID Applying Science to Strengthen and Improve Systems (ASSIST) Project, which is funded by the American people through USAID's Bureau for Global Health, Office of Health Systems. The project is managed by URC under the terms of Cooperative Agreement Number AID-OAA-A-12-00101. URC's global partners for USAID ASSIST include: EnCompass LLC; FHI 360; Harvard T. H. Chan School of Public Health; HEALTHQUAL International; Initiatives Inc.; Institute for Healthcare Improvement; Johns Hopkins Center for Communication Programs; and WI-HER, LLC.

For more information on the work of the USAID ASSIST Project, please visit www.usaidassist.org or write assist-info@urc-chs.com.

Recommended citation

Broughton E. 2016. Cost-effectiveness of an intervention to increase immunization coverage in Pakistan. *Research and Evaluation Report*. Published by the USAID ASSIST Project. Bethesda, MD: University Research Co., LLC (URC).

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Acronyms

ASSIST	USAID Applying Science to Strengthen and Improve Systems Project
CFP	Community Focal Person
CFR	Case Fatality Rate
CI	Confidence Interval
DALY	Disability-adjusted Life Year
DHO	District Health Officer
EPI	Expanded Program on Immunization
GOS	Government of Sindh Province
GOSDOH	Government of Sindh Department of Health
HSS	Health Systems Strengthening
ICER	Incremental Cost-effectiveness Ratio
IP	Implementing Partner
JSI	John Snow International Research & Training Institute, Inc.
JSO	Junior Social Organizer
LHW	Lady Health Worker
MCH	Maternal & Child Health
MCSP	Maternal and Child Survival Program
MLM	Mid-Level Management
POL	Petroleum, Oils and Lubricants
RSPN	Rural Support Program Network
TT	Tetanus Toxoid
USAID	United States Agency for International Development
VO	Village Organization
WHO	World Health Organization

Executive Summary

Introduction

Immunization coverage in Pakistan remains low at 54% nationwide and 39% in Sindh Province in 2012 [1, 2] despite recent efforts by provincial and national Ministries of Health. Reasons include a lack of political commitment, unreliable vaccine supplies, high cost, lack of motivation among Expanded Program on Immunization (EPI) staff, and a scarcity of data present coverage rates, the size of the birth cohort and the incidence of vaccine-preventable diseases [3, 4]. The Government of Sindh Province in Pakistan sought technical assistance from the USAID-funded Health Systems Strengthening Project to improve immunization uptake in four low-coverage districts of Jacobabad, Kashmore, Tharparkar, and Thatta. This evaluation estimated the effectiveness and efficiency of the intervention to increase immunization uptake and thereby improve population health. It used cost-effectiveness analysis from both the USAID and health system perspectives.

Methods

This retrospective analysis used program effectiveness data routinely collected by the implementing partner, John Snow International (JSI), and cost data collected retrospectively from accounting records. In the health system perspective analysis, all of the costs from the primary analysis were included in addition to health system costs for treating those infected with the vaccine-preventable conditions.

Routine immunization program data included the number of children and pregnant women registered and the number immunized. Using data from epidemiological studies, we estimated the number of cases of vaccine-preventable disease expected to be avoided with immunization and determined the disability-adjusted life years (DALYs) attributable to cases of each vaccine-preventable disease. Cost-effectiveness was calculated using decision-tree analysis.

Program Description

Activities began in February 2014 and continued through June 2016. The JSI team provided technical support for capacity development to the staff of Rural Support Program Network (RSPN), the organization contracted to support local implementation of the program. These staff were trained to:

1. Provide orientation and technical refresher training for vaccinators and supervisors;
2. Conduct Mid-Level Management (MLM) courses for district health management staff;
3. Develop standardized supervision tools for supervisors;
4. Design monitoring and evaluation tools to measure immunization program performance.

Field staff were trained on the significance of routine immunization, cold chain equipment, vaccine supply management, supervisory monitoring checklists to monitor EPI, roles and responsibilities of district MLMs, and registration of children and pregnant women. They also worked to improve monitoring and evaluation and engage village-level local support organizations. Social mobilization activities with Lady Health Workers and Community Focal Persons worked to dispel myths and superstitions related to immunization and promote uptake. Orientations and refresher training courses were provided for vaccinators. They were also given motorcycles to access remote site to provide immunizations.

MLM training involved improving cold chain systems, improving data collection and reporting, promoting community outreach, and ensuring quality services and sustainability.

Results

Since its inception in February 2014, the total cost to USAID of the immunization promotion program implemented in these four districts was US$1.56 million. About 440,000 children and 120,000 women were immunized through the program at an overall cost of $2.80 per vaccination completed. This is around 8% of the Pakistan government spending on health per capita reported in 2012 ($34 per person [5]). The overall incremental cost-effectiveness ratio (ICER) comparing it to business-as-usual, from the USAID perspective, was $1.30 per DALY[1] averted. From the Government of Sindh Department of Health perspective, the program decreased costs while improving health because of the reduced expenditure overall by not treating the number of vaccine-preventable disease cases averted.

From the Government of Sindh's perspective, the program is cost-saving while improving population health even if they implemented the program with their own personnel and achieved very modest improvements in vaccination coverage for children under two years and pregnant women.

Conclusion

Considered from the perspective of an external funder such as USAID, the program is considered cost-effective by the benchmarks of the World Bank and WHO[2] from the USAID perspective. The relative efficiency of the program supports its implementation more widely in other parts of Pakistan, particularly where immunization uptake remains low. The relatively low cost per DALY averted suggests the health system could have a large impact on the welfare of women and children with modest investment.

[1] DALYs are a measure of overall disease burden expressed as the total number of years lost due to ill-health, disability or early death.

[2] The World Bank has a benchmark of $150 per DALY averted for low income countries (insert WB reference) and WHO considers interventions highly cost-effective if their ICER is less than GDPPC (insert WHO reference).

I. Introduction

The Government of Sindh Province (GOS) in Pakistan has made efforts over several years to improve immunization coverage among children and pregnant women to reduce vaccine-preventable diseases. However, vaccination coverage in these populations has remained low (Khan, 2013 WHO 2016). In response, in 2013 the GOS Department of Health sought assistance from the Health System Strengthening (HSS) Project in Pakistan to provide technical assistance to improve immunization uptake in the four low-coverage districts of Jacobabad, Kashmore, Tharparkar, and Thatta.

The initial situational analysis conducted in the four districts identified several challenges in the existing immunization program, including a lack of political commitment at the provincial level, unreliable vaccine supplies, high end-user cost, lack of motivation among Expanded Program on Immunization (EPI) staff, and a scarcity of monitoring, evaluation and reporting data. The USAID implementing partner, John Snow International Research & Training Institute, Inc. (JSI), began a program following the situational analysis to address the identified problems. Elements of the intervention are given in the next section.

The immunizations recommended for children in Pakistan and delivered by this program are for prevention of diphtheria, pertussis, tetanus, tuberculosis, haemophilus influenza B, hepatitis B, pneumococcal pneumonia, measles, and polio. For pregnant women, the program focused on tetanus toxoid (TT) vaccination.

There is no credible dispute that basic childhood immunization is among the most highly cost-effective public health interventions currently available (McGovern and Canning, 2015). What is less clear in some settings, such as Pakistan, is the cost-effectiveness of improving the health system to increase proportion of the population that receive this health service to levels on par with regional or global norms (Pervaiz et al., 2015).

The primary objective of this evaluation was to determine the effectiveness of the program in terms of the increase in immunization uptake and the consequent estimated effects this will have on the target population. It also examined the costs of implementing the program from the perspective of the funder, USAID, to estimate incremental cost-effectiveness of the program compared to the business-as-usual scenario. A secondary analysis determined the cost-effectiveness of the same program from the health system perspective, considering if the funder was an integral, rather than external, part of the health system.

II. Methods

This retrospective analysis used program effectiveness data collected by the implementing partner (IP) as part of their routine monitoring and evaluation of the program. Costs were collected retrospectively from the accounting records of the IP for the entire period beginning with set-up period in 2014 until June 2016. This includes an actual immunization implementation period of two years. Inputs on the changes in incidence of the vaccine-preventable diseases and their case fatality rates were gathered from peer-reviewed literature or other epidemiological published references from sources recognized as reliable. Cost-effectiveness was calculated using decision-tree analysis. Two separate decision trees were used: one to compare the tetanus toxoid immunization program component for pregnant women to business-as-usual, and the other compared the routine childhood immunization program component to business-as-usual (**Appendices 1** and **2**). We used three different perspectives separately for the calculations. The first was the program funder, in this case USAID. The second was the health system perspective under the assumption that they used an IP to implement the program and incurred the same costs as USAID did but also were subjected to the differences in the cost of treating cases of vaccine-preventable diseases. The third consideration was using projections for costs and effectiveness if the program was implemented by the Provincial MOH using their own personnel rather than using an implementing partner.

Results of the two separate analyses for childhood and pregnant women were then combined, given they were implemented together using the same resources (**Table 1**). All analyses were conducted using STATA 13 and TreeAge software.

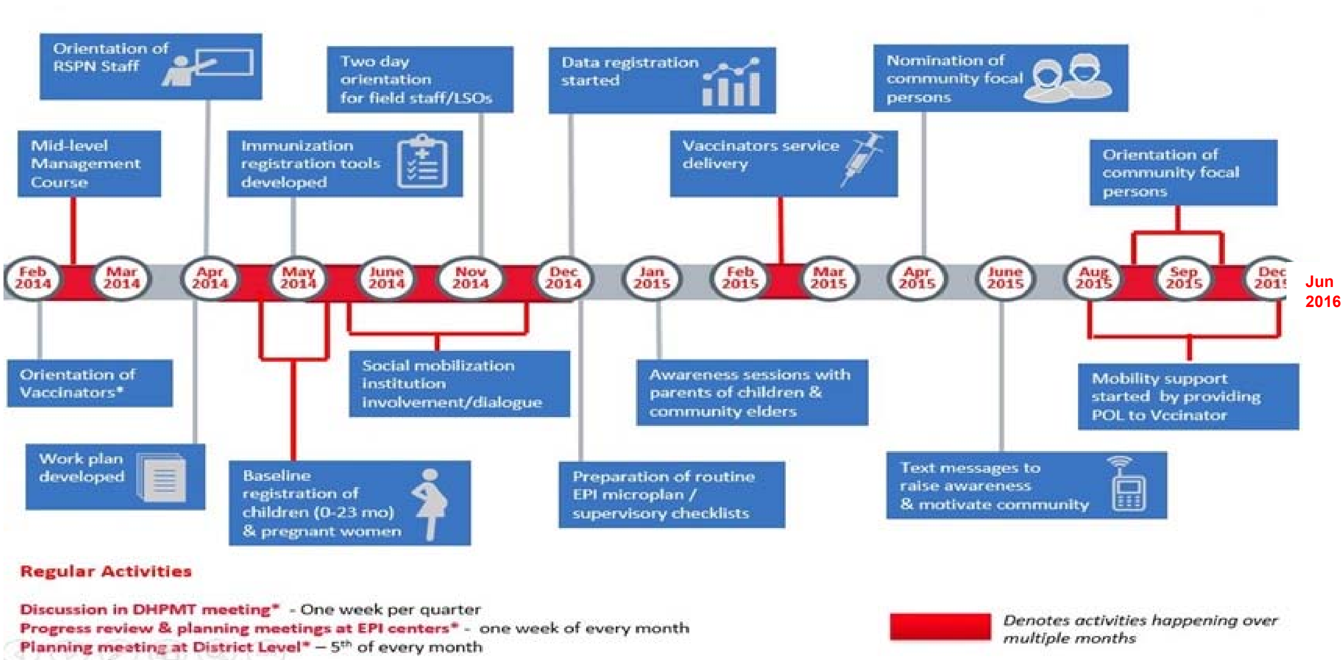
Table 1. Guide for cost-effectiveness analyses conducted

Analysis	Vaccination Program	Perspective	Cost Inputs	Effects Inputs
1 (a)	Children under 2 years	USAID	IP funding	Empirical (from IP)
1 (b)	Pregnant women			
2 (a)	Children under 2 years	GOSDOH (1)	IP funding + treating vaccine-preventable cases	Empirical (from IP)
2 (b)	Pregnant women			
3 (a)	Children under 2 years	GOSDOH (2)	Projected GOSDOH costs + treating vaccine-preventable cases	Sensitivity analysis with lower coverage than IP
3 (b)	Pregnant women			

A. Overview of the Immunization Program Improvement Intervention

Activities began in February 2014, with baseline data collected in May of that year, and continued through June, 2016 (**Figure 1**). The IP team provided technical support to train the Rural Support Program Network (RSPN) staff to perform activities essential for improving immunization coverage.

Figure 1. Immunization intervention timeline



Program activities included:

1. Providing orientation and technical refresher trainings for vaccinators and supervisors;
2. Conducting Mid-Level Management (MLM) courses for district health management staff;
3. Developing standardized supervision tools for supervisors;

4. Cultivating community support and demand for immunization;
5. Designing monitoring and evaluation tools to measure immunization program performance.

It was the Government of Sindh Department of Health (GOSDOH) staff who participated in the MLM training and it was these individuals who managed all of the immunization activities.

Two MLM courses were conducted to update their knowledge using the WHO EPI MLM training modules. Each session included 26 managers. The MLM trainings helped district managers to develop and monitor micro-plans of vaccinators. These micro-plans detailed the dates and locations where the immunizations were to take place and the number and type of vaccines to have available. Other elements covered in the MLM course included:

1. Improving the cold chain system, ensuring proper handling and maintaining cold chain system for safe storage of vaccines
2. Improving the quality of recording and reporting data
3. Creating awareness among community to minimize refusals
4. Ensuring the quality of EPI service deliveries for program sustainability

As part of this program, USAID donated 550 motorcycles to the GOSDOH to improve EPI coverage across the province. The handover of ownership was completed in November 2014. During the period when there was no funding available at the district level for the purpose, the project also provided fuel and other essential supplies to maintain the motorcycles in use to transport vaccinators to sites where they deliver immunizations.

JSI organized a two-day orientation session for RSPNs field staff to explain the immunization program. Participants were briefed on the significance of routine immunization, cold chain equipment, vaccine supply management, use of supervisory checklists to monitor EPI-related activities, and the roles and responsibilities of district health management teams. Through mock exercises, the RSPN staff learned how to register children aged 0 to 24 months and pregnant woman. Participants were trained to conduct contact tracing to locate those lost to follow-up. This enabled RSPN staff to structure their work activities for registering and tracking the target population. A one-day orientation workshop was also conducted for local support organizations. Participants were briefed on the importance of vaccination and the community's role in providing support to EPI to improve coverage.

Orientation sessions and refresher training courses for vaccinators and supervisors were also held. Contents included immunization service delivery techniques, planning immunization schedules, injections and waste disposal safety, cold chain management, data accuracy, and identifying and following up children and pregnant women who had defaulted.

At the village level, local support organizations were designated as responsible for reviewing issues of accessing immunization services and how they could be resolved. They provided information to the community on the importance of improving immunization coverage and general health. They also identified a community focal person (CFP) from each community to support local vaccinators. These unpaid community representatives were responsible for:

1) Informing parents and pregnant women about the arrival of vaccinators;
2) Informing the vaccinator of new births and pregnancies in their catchment; and
3) Ensuring that immunization cards were retained at the community level.

A well-designed social mobilization plan was developed to instigate a change process within the target communities, motivating them to bring their children and pregnant women for vaccination and dispelling myths and superstitions related to immunization. Social Mobilization Officers from RSPN and Lady Health Workers (LHWs) conducted awareness sessions. CFPs also worked with RSPN field teams to educate communities through text messages on the importance of immunization (i.e., types of immunization available, schedules for vaccination, and other pertinent health information) and obtaining and retaining the immunization card as a permanent, personal health record.

B. Model Input Data

Each of the six cost-effectiveness models listed in **Table 1** requires data from various sources. Data on effectiveness of the program in terms of the numbers of women and children vaccinated as well as the direct costs of implementing the program were obtained from the IP. Estimates for incidence of the vaccine-preventable diseases with and without vaccination, and case fatality rates, were obtained from published epidemiological data sources. Pakistani data were used where they were available. Costs for treatment of cases of the diseases considered here were estimated from the experience of experts. Given that Pakistan does not have as health system well-endowed with accurate, reliable and up-to-date service delivery and cost data, the models used in the analysis were simplified.

1. Vaccination Coverage Data

The IP team, in close coordination with GOSDOH and RSPN field staff, developed new monitoring and evaluation tools to track service delivery performance and adverse events. Registration of pregnant women and children under two years of age was an on-going process designed to capture all new pregnancies and births. The CFPs, assisted by Junior Social Organizers (JSOs), went door-to-door in all areas of the participating districts. They also worked with LHWs in areas where they were active. They asked a responsible person in the household for any individuals living there who were children under 24 months of age or women who were currently pregnant. They also collected information including: the child's name, father's name, date of birth/age of the child at the time of registration, sex, the child's vaccination status with different antigens, and availability of the child's vaccination card. If a card was available, the child's vaccination status was copied from that. Based on the vaccination status of children, vaccinators prepared routine EPI micro-plans for the area that included the name of the village to be covered, the target number of children and women to be vaccinated including defaulters, new births, the vaccinator's name and the CFP responsible for providing support, the vaccination schedule, and a suitable place for vaccination to be conducted within the community. The RSPN teams regularly validated reports provided by vaccinators by visiting targeted communities and spot-checking immunization status reports of children. The JSI HSS Project's immunization specialist and the Monitoring and Evaluation Manager also validated data collected and registered children who were not registered during the initial round.

Vaccinators continuously updated the vaccination status of children in permanent registers, and quarterly performance reports based on these registers were submitted to the IP. A routine validation process was undertaken by the IP to monitor each vaccinator's performance and validate the immunization data and the retention of immunization cards by households.

2. Cost Data

The perspective taken for the primary analysis was that of the program funder, USAID. It included all staff time used by the implementing partner to train the RSPN staff, the cost of transportation to the sites to deliver the training, and associated administrative costs. It also included expenses incurred and paid for by the project for RSPN staff involvement in the training, such as their transportation cost and any per diems for overnight travel. A large expense of the program's implementation was the purchase of motorcycles and petroleum and other products required to keep them functioning to transport vaccinators to remote sites where they performed their duties (**Table 2**). From the USAID perspective (Analyses 1 (a) and (b), **Table 1**) the purchase of the motorcycles was considered as a one-off cost because it involved the transfer of ownership to the GOSDOH. For the health system perspectives (Analyses 2 and 3, **Table 1**) we included the depreciation of the vehicles over a period of one year calculated at full straight-line depreciation over five years. All costs are reported in 2015 US dollars with a 3% discount rate applied to future costs.

Table 2. Costs of intervention to implementing partner (in US$)

Line Items	12/2015	1/2016-3/2016	4/2016-6/2016
RSPN teams (Women/children registration, awareness creation etc.)	859,640	191,678	194461
Trainings	15,952	0	0
Coordination meetings	10,032	2,021	0
Motorcycles (USAID perspective)	143,788	0	0
Motorcycles (MOH perspective)*	28758*	6974*	6974*
MLM training and vaccinator orientation	21,790	0	0
Consultation fee including field supervision and monitoring	46,004	5715	0
Mobilization of vaccinators (fuel, etc.)	34,059	17,172	17,171
Total	**1,131,265**	**216,586**	**211,632**

*These figures are not included in the totals for the program's up-front cost.

With all USAID and GOSDOH analyses, we did not include the salary cost for the vaccinators because this was their normal working activities and was not reimbursed by the project. For the USAID perspective, we did not include the cost of the vaccines used because this was borne by the GOSDOH EPI program and not the project. However, we did include this for Analyses 2 to 3. For Analysis 3 from the GOSDOH perspective we included costs paid through the EPI Program for GOSDOH staff to implement the intervention (including MLM capacity development) at an estimated additional 30% cost to the operations and vaccine costs (**Table 3**). An important factor in Analyses 1 (a) and (b) is that they did not include treatment costs that would have been incurred by those in the population under consideration who contracted any of the vaccine-preventable diseases. Treatment costs for those who contracted one of the diseases would have been incurred by both the GOSDOH and the individual and their family. Estimates for the GOSDOH costs were included. Out-of-pocket expenses paid by patients and their families were not included in any of these analyses.

Table 3. Costs of the implementation to Government of Sindh Department of Health

	Projected EPI Spending for 2015 - 2020: Sindh[1]	Estimated for 2015 + 2016, all Sindh[2]	Estimated amount for 4 target districts[3]	Estimated amount for intervention activities[4]	Estimated amount per capita in target population[5]	Sensitivity analysis range[6]	
						Low	High
Operations	54,040,000	21,616,000	2,406,758	722,027	1.29	0.65	1.94
Vaccines	23,600,000	9,440,000	1,051,064	315,319	0.56	0.28	0.85

[1]From GOSDOH EPI data [6].
[2]Based on estimate of 40% in 2015 US$.
[3]Based on Province of Sindh District population data [7].
[4]Based on an 30% increase in projected EPI costs resulting from implementation of the program
[5]Total four-district cost divided by the number in the targeted population from IP registration data
[6]Sensitivity analysis range +/- 50% of the per-capita point estimate.

In the health system perspective analyses, all costs in the primary analysis were included in addition to the costs to the health system of treating those projected to be infected with the vaccine-preventable conditions. These amounts were estimated from public health experts familiar with medical treatment of these diseases in this context and based on their experience of the average fatal and non-fatal cases treated in a public hospital and/or in an outpatient setting (**Table 4**). Because the point estimates are averages, they account for the fact that some children will not be treated within the health system. We assumed a triangular distribution with upper and lower bounds of about one third from the point estimate to account for the uncertainty of the true value for each of these inputs into the model.

Table 4. Estimated cost to health system of treating vaccine-preventable diseases (US$)

Condition	Point estimate	Distribution
Maternal tetanus	1500	Triangular 1000 – 2000
Childhood tetanus	1000	Triangular 500 – 1500
Childhood pertussis	150	Triangular 100 – 200
Childhood diphtheria	150	Triangular 100 – 200
Childhood pneumococcal pneumonia	150	Triangular 100 – 200
Childhood polio	1500	Triangular 1000 – 2000
Childhood measles	500	Triangular 300 – 800
Childhood tuberculosis	1500	Triangular 1000 – 2001
Childhood hepatitis B	1000	Triangular 500 – 1500
Childhood Haemophilus influenza B: invasive	300	Triangular 100 – 500
Fatal case of vaccine-preventable disease	1500	Triangular 1000 – 2000

3. Effectiveness Data

The project collected routine immunization program data on outcome indicators, including:

- Number of children <2 years of age and pregnant women who were registered;
- Percentage of children <2 years of age and pregnant women who were vaccinated;
- Percentage of children <2 years of age and pregnant women who had retained their immunization card.

While it is likely that there were a number of children over two years of age who were vaccinated, they were not included in this indicator if their age was known. For the proportion vaccinated, the numerator included the number of vaccinated children and pregnant women, and the denominator is composed of the total cumulative number of registered children and pregnant women at the end of each quarter. It was RSPN workers along with community focal persons who conducted a household survey census to register all children in these districts for the purpose of this immunization activity.

Using data derived from epidemiological studies, we estimated the number of cases of vaccine-preventable disease expected to be avoided with the increased immunization levels achieved by the program. Where possible, for comparison to the business-as-usual situation, we used epidemiological studies from Pakistan or similar settings for incidence and consequences of the diseases in question (**Table 4**). The distributions were assigned based on the sample size used in the source study or an approximation thereof if it was not stated. These estimates do not account for the effect of herd immunity in the population because data are not available for the total number in the cohort of interest to determine overall population coverage. The studies used as sources for these data are observational studies from Pakistan or similar contexts. There was also no accounting for the proportion of children and pregnant women who may have received an ineffective vaccination dose and not developed the full immunity expected.

For the analyses that used DALYs as their denominator, the figures for burden of disease were estimated from standard cases of the disease reported in the burden of disease literature (**Table 5**) [8]. A 3% discount rate was used for calculating the DALY burden of death of a child under two years of age to match the discounting used for the costs, as is standard practice in economic analysis studies [9].

Data on the number of children and pregnant women who received immunization in the course of the program were given by JSI, the implementing partner. The exact population of these districts is not known, as there has not been a population census since 1998 in this region of the country.

Table 5. Epidemiological inputs for cost-effectiveness model

Variable		Point estimate	Distribution	Source
Case fatality ratio	Diphtheria	0.150	Binomial	Hamborsky et al., 2015 [10]
	Haemophilus influenza B	0.045	Binomial	Hamborsky et al., 2015 [10]
	Hepatitis B	0.010	Binomial	Hamborsky et al., 2015 [10]
	Measles	0.288	Binomial	Khan et al., 2015; Zahidie et al., 2014 [11, 12]
	Pertussis	0.001	Binomial	Hamborsky et al., 2015 [10]
	Pneumococcal pneumonia	0.060	Binomial	Hamborsky et al., 2015 [10]
	Polio	0.035	Binomial	Hamborsky et al., 2015 [10]
	Tetanus	0.301	Binomial	Lambo et al., 2011a; Lambo et al., 2011b [13, 14]
	Tuberculosis	0.43	Binomial	Fatima et al., 2014; Roy et al., 2014 [15, 16]
Probability of disease with no vaccination	Diphtheria	0.00001	Binomial	Iyer et al., 2014 [17]
	Haemophilus influenza B	0.0008	Binomial	Zaidi et al., 2010 [18]
	Hepatitis B	0.150	Binomial	Hamborsky et al., 2015 [10]
	Pertussis	0.0015	Binomial	Hamborsky et al., 2015 [10]
	Pneumococcal pneumonia	0.010	Binomial	Hamborsky et al., 2015 [10]
	Polio	0.000013	Binomial	Ghafoor and Sheikh, 2016
	Tetanus	0.0008	Binomial	Lambo et al., 2011a; Lambo et al., 2011b [13, 14]
	Tuberculosis	0.004	Binomial	Fatima et al., 2014; Roy et al., 2014 [15, 16]
Probability of disease with vaccination	Diphtheria	0.0000004	Binomial	Hamborsky et al., 2015 [10]
	Haemophilus influenza B	0.00004	Binomial	Hamborsky et al., 2015 [10]
	Hepatitis B	0.0075	Binomial	Hamborsky et al., 2015 [10]
	Pertussis	0.0003	Binomial	Hamborsky et al., 2015 [10]
	Pneumococcal pneumonia	0.001	Binomial	Hamborsky et al., 2015; Owais et al., 2010 [10, 19]
	Polio	0.00000063	Binomial	Hamborsky et al., 2015 [10]
	Tetanus	0	Binomial	Hamborsky et al., 2015; Lambo et al., 2011a; Lambo et al., 2011b [10, 13, 14]
	Tuberculosis	0.00076	Binomial	Fatima et al., 2014; Roy et al., 2014 [15, 16]
Probability of death from other causes		0.0372	Binomial	WHO 2004 [5]

C. Cost-effectiveness Calculation Method

Probabilities of receiving vaccination and contracting the vaccine-preventable diseases and expected payoff in terms of cases of the diseases, DALYs, and disease treatment costs were entered into the models, mostly as probability distributions according to **Tables 2, 3, 4** and **5.** Monte Carlo simulations were run to arrive at a point estimate and credibility interval, taking into account the input values' distributions (**Table 6**). Population size data were collected from JSI from their routine program monitoring data (**Table 7**). This is the commonly used method to account for uncertainty in the input variables in the model to be reflected in the outcomes [8,20].

Table 6. Disability-adjusted life year values for vaccine-preventable diseases

Parameter		Point estimate
DALY effect of disease	Diphtheria	0.231
	Fatality	32.7
	Haemophilus influenza B	0.41
	Hepatitis B	0.075
	Measles	0.152
	Pertussis	0.175
	Pneumococcal pneumonia	0.146
	Polio	0.369
	Tetanus	0.638
	Tuberculosis	0.333

Table 7. Population coverage from the immunization program

Parameter	Estimate	Distribution
Probability of child receiving immunization before program	0.35	Binomial
Probability of child receiving immunization before program	0.75	Binomial
Total number of children receiving immunization	329174	
Estimated number of children	438899	
Total number of pregnant women receiving TT immunization	111377	
Total number of pregnant women eligible for immunization	119800	
Probability pregnant woman received TT immunization before program	0.25	

Source: JSI program data.

III. Results

The total cost of the program from the perspective of the program funder, USAID, was US$1.56 million for all activities since its inception in February 2014. The total number of children reportedly provided routine childhood immunization through the program was over 329,000, and the total number of pregnant women receiving tetanus toxoid (TT) vaccination over the same period was over 111,000. From the perspective of USAID, the incremental cost-effectiveness ratio (ICER) of the program compared to our estimate of the business-as-usual scenario was US$1.30 per DALY averted (95% CI: US$1.08 – 1.58) (**Table 8**). Including estimates of the cost to the health system of treating vaccine-preventable morbidity and mortality from the perspective of the health system that would incur such costs, the ICER is about -US$97 per DALY averted (95% CI: -US$129 –(-US$66)). This means that from the health system perspective, the program improved public health by decreasing morbidity and mortality from vaccine-preventable diseases while also saving the health system money by eliminating the treatment costs of those cases of morbidity and mortality averted from the vaccination promotion program. From the USAID perspective, the cost of the program is just over US$3,000 per life saved.

These results are plausible and have internal validity as verified by sensitivity analysis. For example, an increase in the cost of the intervention is expected to make the intervention less cost-effective and this was found to be the case when this input was varied when conducting sensitivity analysis (see next section).

Table 8. Incremental cost-effectiveness ratio results (cost in 2015 USD)

Population	**Perspective**	**Point estimate (ICER)**	**95% CI (ICER)**		**Unit**
			Lower	Upper	
Children	USAID	1.30	1.08	1.58	Cost/DALY
Pregnant women	USAID	2404	1919	3765	Cost/DALY
Total	USAID	1.30	1.08	1.58	Cost/DALY
Children	GOSDOH	-97	-129	-68	Cost/DALY
Pregnant women	GOSDOH	2244	1975	2576	Cost/DALY
Total	GOSDOH	-92.98	-121.09	-66.25	Cost/DALY

Note: Negative numbers means that the intervention is “dominant” or it decreases costs while also improving health.

A. Return on Investment

Given that the program is cost-saving from the GOSDOH perspective if they paid for the intervention alone, it can be logically inferred that if USAID or another donor mechanism was to pay for the implementation, it would be even more cost-saving for the GOSDOH. From this model, the $1,56 million initial investment in the program would save the GOSDOH more than $10 million. Even using very conservative estimates for the effectiveness of the program. The expected cost-savings for the GOSDOH would be several million dollars. The strongly suggests the program would be sustainable over the long term.

B. Sensitivity Analysis

We conducted one-way sensitivity analyses by increasing each of the inputs in turn by 10%, then determining the effect this would have on the overall ICER measure of cost-effectiveness. We did this separately for both the childhood vaccination and the pregnant women TT vaccination models (**Tables 9** and **10**). An example of the interpretation of the results of the sensitivity analysis is presented in **Table 9**: If the case fatality rate of tetanus increased by 10% (or its real value was 10% higher than the estimate used here in the model), then the ICER result would be 10.84% lower, meaning that the program would be 10.84% more cost-effective than the results shown in **Table 8**.

Table 9. One-way sensitivity analysis for childhood vaccination, health system perspective

Parameter increased by 10%	% change in ICER	Direction
Tetanus case fatality rate (CFR)	-10.84%	More cost-effective
Probability of receiving vaccination if program implemented	-7.47%	More cost-effective
Probability of Hepatitis B with no vaccination	-3.16%	More cost-effective
Probability of contracting tetanus if no vaccination	-2.57%	More cost-effective
Cost of a non-fatal tetanus case	-2.23%	More cost-effective
Cost of a non-fatal Hepatitis B case	-1.03%	More cost-effective
Hepatitis B CFR	-0.10%	More cost-effective
Tuberculosis CFR	-0.09%	More cost-effective
Diphtheria CFR	-0.05%	More cost-effective
Probability of tuberculosis with no vaccination	-0.04%	More cost-effective
Pneumococcal pneumonia CFR	-0.02%	More cost-effective
Probability of pneumococcal pneumonia with no vaccination	-0.01%	More cost-effective
Probability of pertussis with vaccination	0.00%	Negligible change
Probability of tetanus with vaccination	0.00%	Negligible change
Probability of tuberculosis with vaccination	0.00%	Negligible change
Probability of measles with vaccination	0.00%	Negligible change
Probability of diphtheria with vaccine	0.00%	Negligible change
Probability of tetanus with vaccine	0.00%	Negligible change
Pertussis CFR	0.00%	Negligible change
Haemophilus influenza B CFR	0.00%	Negligible change
Probability of pneumoccoccal pneumonia with vaccination	0.00%	Negligible change
Probability of diphtheria with no vaccination	0.00%	Negligible change
Probability of pertussis with no vaccine	0.00%	Negligible change
Probability of measles with no vaccine	0.00%	Negligible change
Probability of haemophilus influenza B with no vaccine	0.00%	Negligible change
Probability of polio with no vaccination	0.00%	Negligible change
Polio CFR	0.00%	Negligible change
Cost of diphtheria case	0.00%	Negligible change
Cost of Hepatitis B case	0.00%	Negligible change
Cost of pertussis case	0.00%	Negligible change
Cost of measles case	0.00%	Negligible change
Cost of haemophilus influenza B case	0.00%	Negligible change
Cosst of pneumococcal pneumonia case	0.00%	Negligible change
Probability of HIB with vaccination	0.00%	Negligible change
Cost of a case of pneumonia in a child	0.00%	Negligible change
Probability of HIB with vaccination	0.00%	Negligible change
Probability of Polio with vaccination	0.00%	Negligible change
Probability to hepatitis B with vaccination	0.16%	Less cost-effective
Probability of vaccination if no IPP	1.14%	Less cost-effective

Table 10. One-way sensitivity analysis for TT vaccination of pregnant women, health system perspective

Parameter increased by 10%	% change	Direction
Probability of receiving vaccination if program implemented	-19.15%	More cost-effective
Probability of contracting tetanus if no TT vaccination	-16.92%	More cost-effective
Tetanus CFR	-8.60%	More cost-effective
Probability of getting TT vaccine with program in place	-3.92%	More cost-effective
Cost of fatal case of tetanus	-1.98%	More cost-effective
Cost of non-fatal tetanus case	-0.14%	More cost-effective
Probability of contracting tetanus with vaccination	0.00%	Negligible change
Cost of registration, creating awareness, etc. for Q2, 2016	0.63%	Less cost-effective
Cost of registration, awareness, etc. for Q1, 2016	0.66%	Less cost-effective
Cost of motorcycle purchase in 2015	0.97%	Less cost-effective
Cost of petrol & maintenance for motorcycles 2015	1.69%	Less cost-effective
Cost of MLM training and vaccinator orientation 2015	1.77%	Less cost-effective
Cost of petrol and maintenance for motorcycles Q1, 2016	1.80%	Less cost-effective
Cost of training in 2015	1.81%	Less cost-effective
Cost of registration, creating awareness etc., 2015	3.71%	Less cost-effective
Cost of coordination meeting 2015	8.54%	Less cost-effective
Cost of consultant in Q1, 2016	8.57%	Less cost-effective
Cost of coordination meetings in Q1, 2016	8.59%	Less cost-effective
Total women of reproductive age	11.39%	Less cost-effective
Gets TT vaccination if no program in place	13.60%	Less cost-effective

The final sensitivity analysis performed was the two-way calculation dome in Analysis 3 using the GOSDOH perspective under the assumption that they implemented the intervention with their own staff. Using the conservative estimate that it would have cost them as much with their own staff as it would have using an IP, we varied the level of effectiveness of both components of the intervention simultaneously downwards until a point where vaccination coverage would be only 4% above (**Table 11**). Even at this unfavorable extreme of low positive effects from the intervention, it was estimated to be cost-saving, meaning the program would produce better health while saving the GOSDOH resources they could use on other health priorities. This means that there would be a positive return on investment even if the program was not as effective as expected from the empirical evidence from the IP.

Table 11. Sensitivity analysis from the Government of Sindh Department of Health perspective with decreasing intervention effectiveness

Vaccination coverage achieved		ICER
Children	Pregnant women	
0.75	0.93	-92.8
0.73	0.90	-91.7
0.71	0.86	-90.5
0.69	0.83	-89.3
0.67	0.79	-88.1
0.65	0.76	-86.9
0.63	0.73	-85.7
0.61	0.69	-84.4
0.59	0.66	-83.2
0.57	0.63	-81.9
0.55	0.59	-80.6
0.53	0.56	-79.3
0.51	0.52	-78.0
0.49	0.49	-76.7
0.47	0.46	-75.4
0.45	0.42	-74.0
0.43	0.39	-72.7
0.41	0.36	-71.3
0.39	0.32	-69.9

IV. Discussion

The immunization promotion program implemented in these four districts between February 2014 and June 2016 provided immunization to about 440,000 children and 120.000 pregnant women out of the target population. The total implementation cost was $1.56 million or $2.80 per child or pregnant woman in the target population. The overall cost-effectiveness comparing the program to business-as-usual from the USAID perspective was US$1.30 per DALY averted. From the GOSDOH perspective, assuming the Government of Sindh paid for the intervention rather than USAID and that implementation achieved the same level of success, the program would be cost-saving due to reduced expenditure on treating vaccine-preventable cases of disease. Therefore, if other provincial department of health were to invest in the same program conducted by the same implementing partner for application in districts where vaccination rates were similarly low as in the four districts targeted here, they could expect to decrease overall costs to the health system from these eight diseases. The cost of the intervention and its effectiveness would change with implementation in different geographical areas and this would need to be taken into consideration in projecting cost-effectiveness to other settings. If the GOSDOH used their own personnel to conduct an intervention of essentially the same design, the program would still produce a major return on investment, even if the level of coverage achieved was much less than that achieved by the IP.

The Pakistan government spending on health was reported to be $34 per person in 2012 [5]. This means that the $2.80 initial cost of this intervention is about 8% of total spending on health and therefore appears affordable as an initial expenditure. The large cost-savings expected from this relatively small expenditure indicates it had an excellent return on investment. This strengthens the case for more widespread adoption of the intervention, at least in similar low vaccine coverage settings.

The ICER results were divided into those for children and pregnant women because this is how the data were collected. However, the immunization promotion program was implemented as one integrated intervention, and the effectiveness and efficiency measures determined here should be considered for the program overall. For example, the motorcycles for transportation of the vaccinators to remote sites to provide their services were considered separately for the children's program and the pregnant women's TT promotion program. However, in reality, only one set of motorcycles was purchased, and vaccinators dispensed both childhood and TT immunizations during the same visits. Therefore, the ICER result for the program overall is lower than the two results for children and pregnant women considered separately. The ICER for pregnant women is much higher because tetanus is a rarer condition than most of the eight other vaccine-preventable diseases for which children are routinely immunized.

Monte Carlo simulations simultaneously vary the input parameters in the model according to their distribution noted above to give a range of results reflecting the uncertainty of the input variables. Given the 95% confidence intervals presented in **Table 8**, we see that there is a reasonable degree of certainty that the program is cost-effective from the USAID perspective or cost-saving from the health system perspective. The one-way sensitivity analyses show that the variables that appear to have the most impact on the overall cost-effectiveness result are the effectiveness of the program in vaccinating those eligible and the proportion who receive vaccination if the program is not in place. Therefore, better or worse relative effectiveness in covering the at-risk population with vaccines appears to be the biggest driver of the efficiency of the program, which is intuitively consistent. It indicates that in using this intervention in other settings, implementation such that the effectiveness reported here is equaled or improved upon is the key element in ensuring the same or better overall efficiency. It also indicates that the overall result of the program being considered cost-effective according to WHO and World Bank benchmarks is not sensitive to feasible changes to the input variables [5, 21]. This indicates the conclusion that the program is cost-effective or cost-saving, depending on the perspective is robust despite uncertainty in the input variables.

The ICERs expressed as dollars per life saved are much higher than those for the results reported for DALYs averted. This is due to the fact that vaccine-preventable diseases as a group do not have very high case fatality rates. Due to this, there were not many deaths averted, and higher costs per life saved. However, there was a large number of cases averted with this program, and considering the burden of non-fatal cases averted gives a much more accurate picture of the program's effectiveness. The sensitivity analyses' results also indicated that changes of 10% to any one specific cost item would not have a significant impact on the overall cost-effectiveness result.

If we had taken the societal perspective for the analysis, the ICER results would have been more favorable because families of children and pregnant women suffer many of the economic consequences of vaccine-preventable morbidity and mortality not captured here by the two perspectives shown. Using the societal perspective would include the out-of-pocket expenses for medical attention and transportation needed to seek care and the opportunity cost of the time taken in caring for the incapacitated family member.

A. Limitations

In some districts participating in the intervention, a small proportion of local populations may have been missed for registration and hence the opportunity for immunization due to travel for harvesting or feeding livestock during the drought period, which occurred during the time of the intervention. As there has been no national census since 1998, it was not possible to compare registration numbers with population estimates of children and pregnant women in the target groups. Despite these limitations, the door-to-door strategy used to capture those eligible for the program is thought to have reached a high proportion of the eligible population.

Given that this setting has very poor data due to the long period since a census and the generally poor health information systems, there was substantial uncertainty in the input variables of the model. While this was accounted for with the data available and estimates derived from similar settings, a stronger national or regional health information system would have provided more accurate information and therefore would have allowed a more precise measure of efficiency.

One reason for the favorable cost-saving result from the analyses from the GOSDOH perspective is the cost of treating those who contract the vaccine-preventable diseases and receive treatment at publicly funded health facilities. This is based on the assumption that all children and pregnant women falling ill with these diseases would seek and receive such treatment. It is likely that a proportion in this group would not seek treatment at public facilities but would opt instead for private practitioners or private dispensaries and some may also go untreated [22-24]. With no data to guide an appropriate input on this proportion, we assumed all ill pregnant women or children would seek some care and used what we considered an appropriate average. While an over-estimate would have biased the result for cost-effectiveness from the GOSDOH perspective favorably, these are economic costs that should be captured in the societal perspective.

V. Conclusion

The relative efficiency of this program in improving the system of immunization for children under 24 months and pregnant women in these four districts in Pakistan compared favorably to WHO norms [21, 25]. It is recommended that it be implemented more widely in other parts of the country, especially where the proportion of the target population immunized remains low. From the USAID perspective, the relatively low cost per DALY averted suggests the health system could have a large impact on the welfare of women and children with a relatively small investment in such a program.

If the GOSDOH was able to develop the management, training, and logistical capacity of their own personnel such that they could achieve the same results as the IP in this case, there would be an excellent return on investment from this program with the overall saving of many millions of dollars. Childhood and maternal immunization is one of the most cost-effective interventions available to public health providers and ensuring their delivery to the population is considered a basic responsibility of any government's health ministry. This evaluation has shown that interventions aimed at strengthening the health system to increase the delivery of life-saving maternal and child immunizations will have a major positive benefit to health while providing a substantial return on investment.

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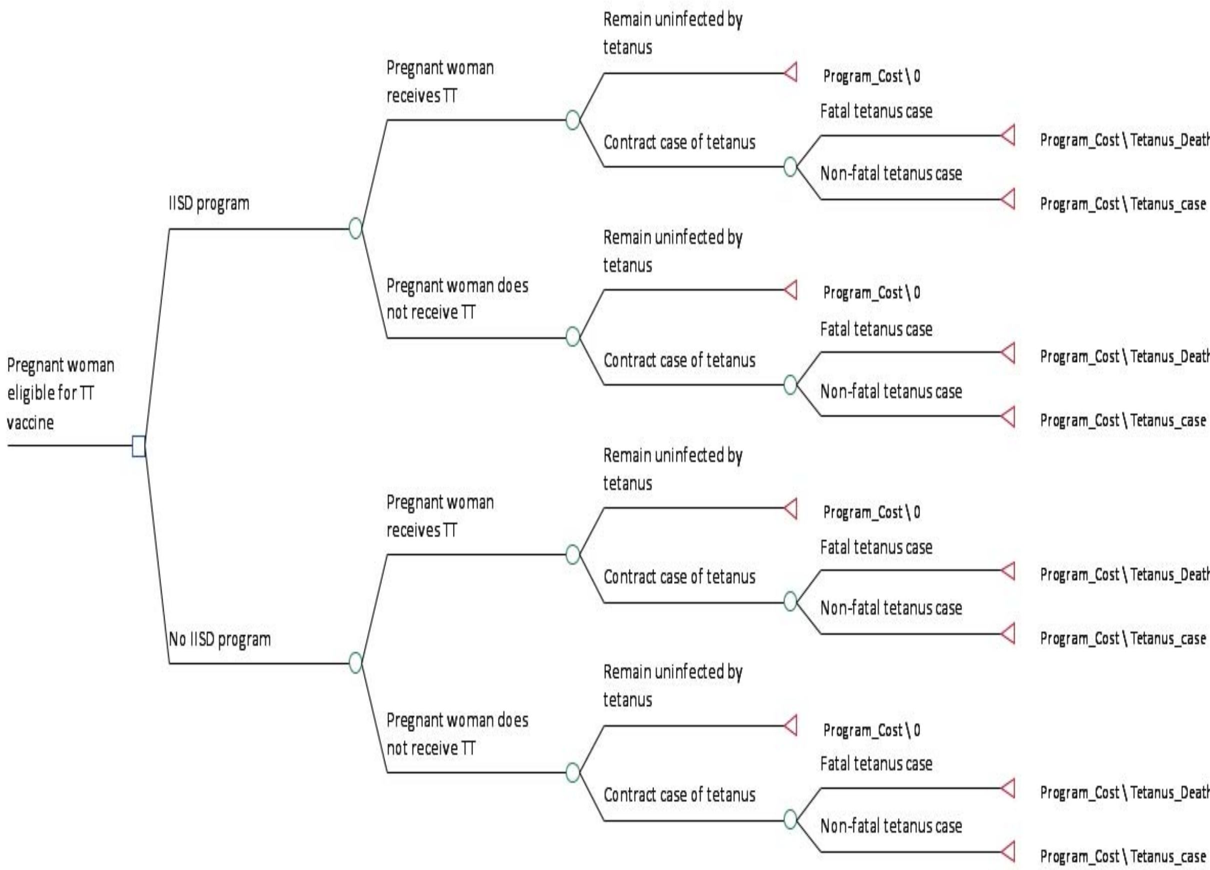
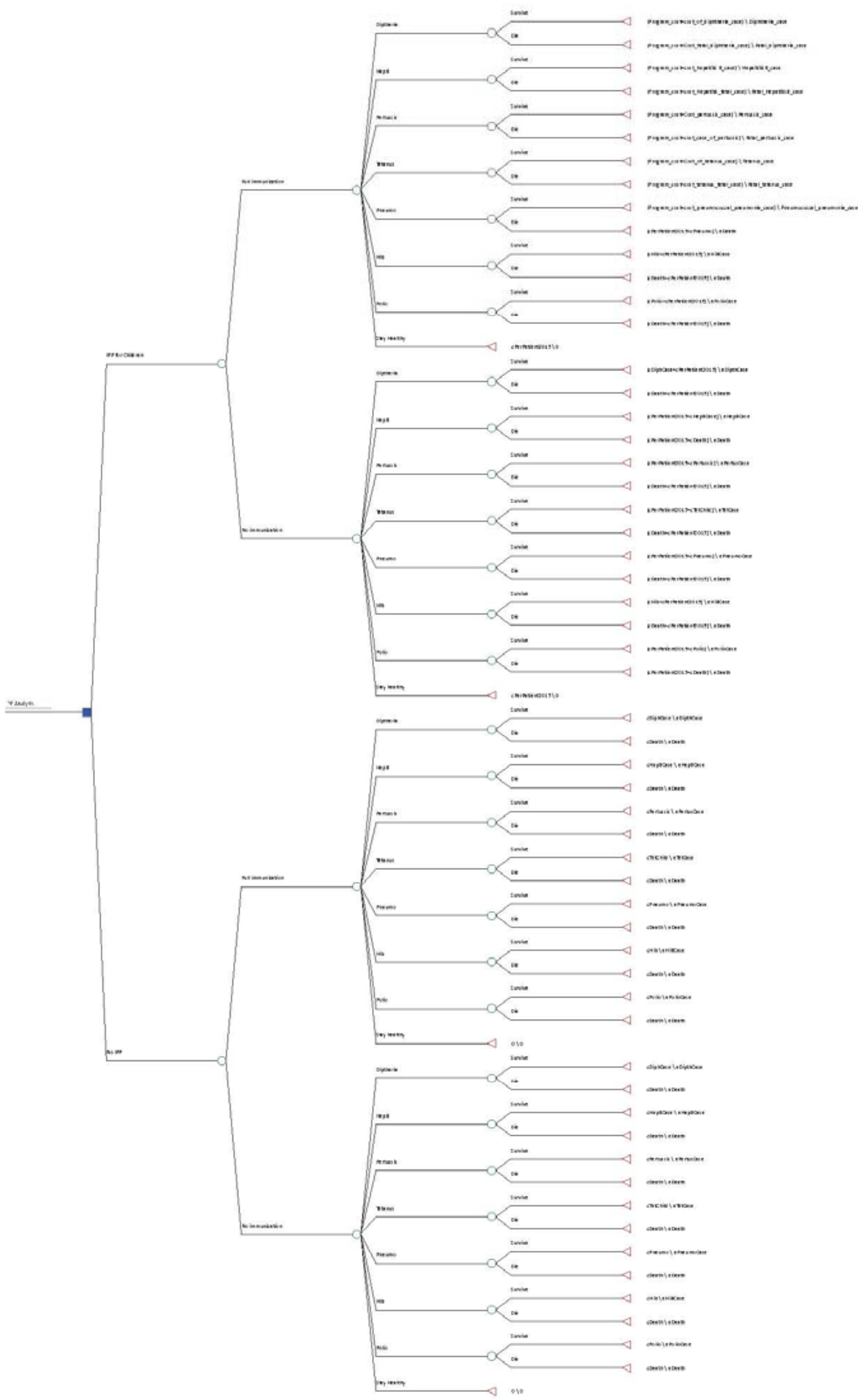
Appendices

Appendix I: Decision Tree for Pregnant Women's Immunization Component



Appendix II: Decision Tree for Children's Immunization Component



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